```
=> d his ful

     (FILE 'HOME' ENTERED AT 14:54:21 ON 21 FEB 2006)

     FILE 'HCAPLUS' ENTERED AT 14:55:06 ON 21 FEB 2006
L1             1 SEA ABB=ON  PLU=ON  US20040122015 /PN
                 D ALL
                 SEL RN

     FILE 'REGISTRY' ENTERED AT 15:04:14 ON 21 FEB 2006
L2            64 SEA ABB=ON  PLU=ON  (108-24-7/BI OR 118486-94-5/BI OR
                 126747-14-6/BI OR 135579-87-2/BI OR 193361-76-1/BI OR
                 33252-28-7/BI OR 41963-20-6/BI OR 468068-39-5/BI OR
                 544-92-3/BI OR 54663-78-4/BI OR 5470-11-1/BI OR
                 619334-28-0/BI OR 619334-29-1/BI OR 619334-30-4/BI OR
                 619334-31-5/BI OR 619334-32-6/BI OR 619334-33-7/BI OR
                 619334-34-8/BI OR 619334-35-9/BI OR 619334-36-0/BI OR
                 619334-37-1/BI OR 619334-38-2/BI OR 619334-39-3/BI OR
                 619334-40-6/BI OR 619334-41-7/BI OR 619334-42-8/BI OR
                 619334-43-9/BI OR 619334-44-0/BI OR 619334-50-8/BI OR
                 619334-51-9/BI OR 619334-52-0/BI OR 619334-53-1/BI OR
                 619334-54-2/BI OR 619334-55-3/BI OR 619334-59-7/BI OR
                 619334-62-2/BI OR 619334-64-4/BI OR 619334-66-6/BI OR
                 619334-67-7/BI OR 619334-68-8/BI OR 619334-70-2/BI OR
                 619334-73-5/BI OR 619334-75-7/BI OR 619334-76-8/BI OR
                 619334-79-1/BI OR 619334-81-5/BI OR 619334-82-6/BI OR
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                 6783-05-7/BI OR 706784-91-0/BI OR 706784-92-1/BI OR
                 706784-93-2/BI OR 706784-94-3/BI OR 706784-96-5/BI OR
                 706784-97-6/BI OR 706784-98-7/BI OR 706784-99-8/BI OR
                 706785-00-4/BI OR 706785-01-5/BI OR 706785-02-6/BI OR
                 77-78-1/BI OR 97483-77-7/BI)
                 D SCAN

     FILE 'LREGISTRY' ENTERED AT 15:05:29 ON 21 FEB 2006
L3               STR

     FILE 'REGISTRY' ENTERED AT 15:17:22 ON 21 FEB 2006
L4            50 SEA SSS SAM L3
                 D QUE STAT
L5         13607 SEA SSS FUL L3
                 SAV L5 DAV525/A

     FILE 'LREGISTRY' ENTERED AT 15:20:23 ON 21 FEB 2006
L6               STR

     FILE 'REGISTRY' ENTERED AT 15:27:09 ON 21 FEB 2006
L7            16 SEA SUB=L5 SSS SAM L6
                 D SCAN
L8           376 SEA SUB=L5 SSS FUL L6
                 SAV L8 DAV525A/A

     FILE 'LREGISTRY' ENTERED AT 15:30:49 ON 21 FEB 2006
L9               STR L3
L10              STR L6

     FILE 'REGISTRY' ENTERED AT 15:37:43 ON 21 FEB 2006
L11            2 SEA SUB=L8 SSS SAM L10
                 D SCAN
L12           50 SEA SUB=L8 SSS FUL L10
                 SAV L12 DAV525B/A
                 D SCAN
L13          326 SEA ABB=ON  PLU=ON  L8 NOT L12

     FILE 'HCAPLUS' ENTERED AT 15:41:31 ON 21 FEB 2006
L14            4 SEA ABB=ON  PLU=ON  L12
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L15          125 SEA ABB=ON  PLU=ON  L13
L16          127 SEA ABB=ON  PLU=ON  L8

     FILE 'REGISTRY' ENTERED AT 15:43:53 ON 21 FEB 2006
L17           30 SEA ABB=ON  PLU=ON  L2 AND L8
                 D SCAN
L18           34 SEA ABB=ON  PLU=ON  L2 NOT L17
                 D SCAN

     FILE 'HCAPLUS' ENTERED AT 15:46:35 ON 21 FEB 2006
L19            4 SEA ABB=ON  PLU=ON  L17
L20            4 SEA ABB=ON  PLU=ON  L14 AND L19

     FILE 'LREGISTRY' ENTERED AT 15:48:54 ON 21 FEB 2006
                 D QUE STAT L8
                 D QUE STAT L9
                 D QUE STAT L10
                 D QUE L6
L21              STR L3
                 D QUE STAT L12
L22              STR L21

     FILE 'REGISTRY' ENTERED AT 15:59:06 ON 21 FEB 2006
L23            2 SEA SUB=L8 SSS SAM (L21 OR L22)
                 D SCAN
L24           70 SEA SUB=L8 SSS FUL (L21 OR L22)
                 SAV L24 DAV525C/A
L25          306 SEA ABB=ON  PLU=ON  L8 NOT L24
L26           20 SEA ABB=ON  PLU=ON  L24 NOT L12
L27           70 SEA ABB=ON  PLU=ON  L24 OR L12

     FILE 'LREGISTRY' ENTERED AT 16:04:18 ON 21 FEB 2006
L28              STR L3

     FILE 'REGISTRY' ENTERED AT 16:06:49 ON 21 FEB 2006
L29            0 SEA SUB=L8 SSS SAM L28
                 D QUE STAT
L30            0 SEA SUB=L8 SSS FUL L28
L31            0 SEA SUB=L5 SSS SAM L28
                 D QUE STAT
                 D QUE STAT L30
L32            4 SEA SUB=L5 SSS FUL L28
                 D SCAN
L33           74 SEA ABB=ON  PLU=ON  L32 OR L27

     FILE 'HCAPLUS' ENTERED AT 16:11:55 ON 21 FEB 2006
L34            7 SEA ABB=ON  PLU=ON  L33
L35            7 SEA ABB=ON  PLU=ON  L34 OR L20
L36       159200 SEA ABB=ON  PLU=ON  (PHARMA? OR DRUG? OR MEDICIN?)(2A)(
                 CARRIER? OR DELIV?)
L37           26 SEA ABB=ON  PLU=ON  L16 AND L36
L38       470215 SEA ABB=ON  PLU=ON  ?MICROB?
L39           26 SEA ABB=ON  PLU=ON  L16 AND L38
L40           43 SEA ABB=ON  PLU=ON  L37 OR L39
L41           47 SEA ABB=ON  PLU=ON  L40 OR L35
L42           40 SEA ABB=ON  PLU=ON  L41 NOT L35
                 D QUE STAT L35



=> => d que stat l35
L2            64 SEA FILE=REGISTRY ABB=ON  PLU=ON  (108-24-7/BI OR
                 118486-94-5/BI OR 126747-14-6/BI OR 135579-87-2/BI OR
                 193361-76-1/BI OR 33252-28-7/BI OR 41963-20-6/BI OR
                 468068-39-5/BI OR 544-92-3/BI OR 54663-78-4/BI OR
                 5470-11-1/BI OR 619334-28-0/BI OR 619334-29-1/BI OR
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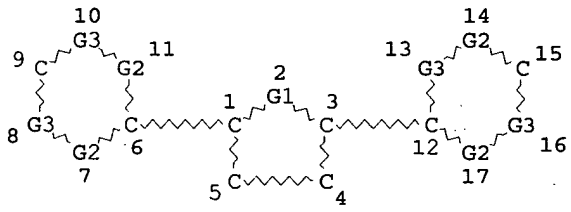
619334-30-4/BI OR 619334-31-5/BI OR 619334-32-6/BI OR
619334-33-7/BI OR 619334-34-8/BI OR 619334-35-9/BI OR
619334-36-0/BI OR 619334-37-1/BI OR 619334-38-2/BI OR
619334-39-3/BI OR 619334-40-6/BI OR 619334-41-7/BI OR
619334-42-8/BI OR 619334-43-9/BI OR 619334-44-0/BI OR
619334-50-8/BI OR 619334-51-9/BI OR 619334-52-0/BI OR
619334-53-1/BI OR 619334-54-2/BI OR 619334-55-3/BI OR
619334-59-7/BI OR 619334-62-2/BI OR 619334-64-4/BI OR
619334-66-6/BI OR 619334-67-7/BI OR 619334-68-8/BI OR
619334-70-2/BI OR 619334-73-5/BI OR 619334-75-7/BI OR
619334-76-8/BI OR 619334-79-1/BI OR 619334-81-5/BI OR
619334-82-6/BI OR 619334-83-7/BI OR 619334-85-9/BI OR
624-28-2/BI OR 6783-05-7/BI OR 706784-91-0/BI OR
706784-92-1/BI OR 706784-93-2/BI OR 706784-94-3/BI OR
706784-96-5/BI OR 706784-97-6/BI OR 706784-98-7/BI OR
706784-99-8/BI OR 706785-00-4/BI OR 706785-01-5/BI OR
706785-02-6/BI OR 77-78-1/BI OR 97483-77-7/BI)

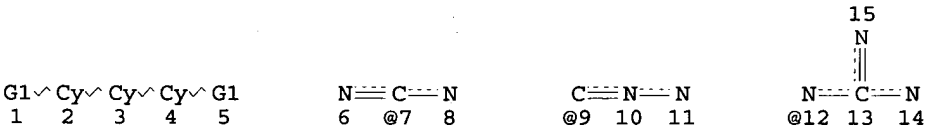
L3 STR



VAR G1=N/O/S
VAR G2=C/N/O/S
VAR G3=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

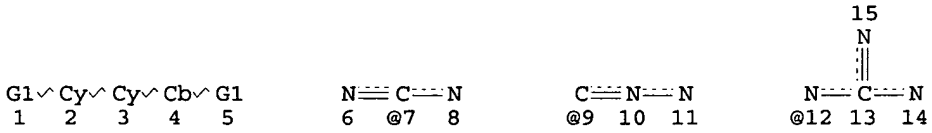
STEREO ATTRIBUTES: NONE
L5 13607 SEA FILE=REGISTRY SSS FUL L3
L6 STR



VAR G1=7/9/12
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

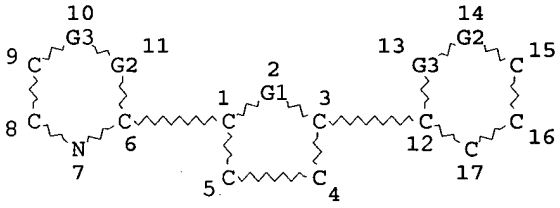
STEREO ATTRIBUTES: NONE
L8 376 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L10 STR



VAR G1=7/9/12
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 2
GGCAT IS UNS AT 3
GGCAT IS UNS AT 4
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E5 C E1 N AT 2
ECOUNT IS E4 C E1 O AT 3
ECOUNT IS E6 C AT 4

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

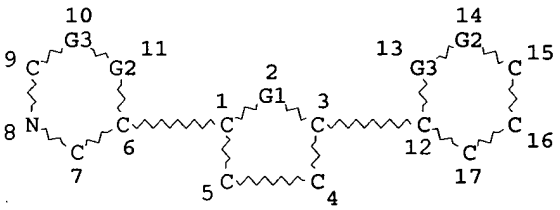
STEREO ATTRIBUTES: NONE
L12 50 SEA FILE=REGISTRY SUB=L8 SSS FUL L10
L14 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L12
L17 30 SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND L8
L19 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L17
L20 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND L19
L21 STR



VAR G1=O/S
VAR G2=C/N/O/S
VAR G3=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L22 STR

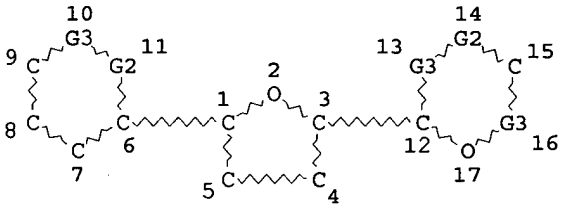


VAR G1=O/S
VAR G2=C/N/O/S
VAR G3=C/N

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L24 70 SEA FILE=REGISTRY SUB=L8 SSS FUL (L21 OR L22)
L27 70 SEA FILE=REGISTRY ABB=ON PLU=ON L24 OR L12
L28 STR



VAR G2=C/N/O/S
VAR G3=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L32 4 SEA FILE=REGISTRY SUB=L5 SSS FUL L28
L33 74 SEA FILE=REGISTRY ABB=ON PLU=ON L32 OR L27
L34 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L33
L35 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L34 OR L20

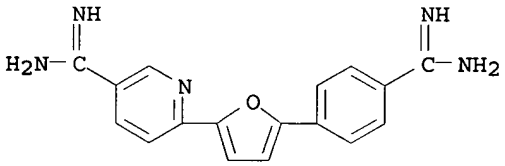
=> d l35 1-7 ibib abs hitstr hitind

L35 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:548369 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 143:221773
TITLE: In vitro metabolism of an orally active O-methyl amidoxime prodrug for the treatment of CNS trypanosomiasis
AUTHOR(S): Ansede, J. H.; Voyksner, R. D.; Ismail, M. A.; Boykin, D. W.; Tidwell, R. R.; Hall, J. E.
CORPORATE SOURCE: Division of Drug Delivery and Disposition, School of Pharmacy, The University of North Carolina at Chapel Hill, Chapel Hill, USA
SOURCE: Xenobiotica (2005), 35(3), 211-226
CODEN: XENOBH; ISSN: 0049-8254
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new aza-analog of furamidine, 6-[5-(4-amidinophenyl)-furan-2-yl]nicotinamidine (DB820), has potent in vitro antitrypanosomal activity; however, it suffers from poor oral activity because of its pos. charged amidine groups. The dimethoxyamidine prodrug of DB820, N-methoxy-6-{5-[4-(N-methoxyamidino)phenyl]-furan-2-yl}-nicotinamidine (DB844), has potent oral activity in mouse models of both early-stage and CNS African trypanosomiasis. Metabolism of DB844 in human liver microsomes (HLM) was investigated using liquid chromatog.-mass spectrometry (LC-MS/MS). The metabolism of DB844 in

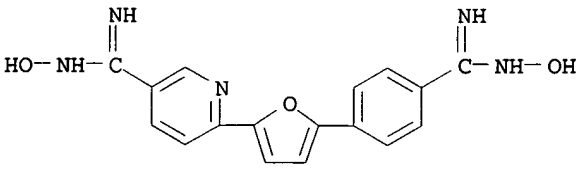
HLM was NADPH-dependent and resulted in the production of eight metabolites over a 90 min incubation. O-Demethylation and N-dehydroxylation reactions resulted in the metabolic conversion of DB844 to its active DB820 metabolite. Chromatog. conditions used for LC-MS anal. allowed for the separation and identification of all metabolites including positional isomers. Demethylation of either the Ph or pyridine side of DB844 (DB844 m/z 366.2) resulted in the production of two metabolites (M1A, M1B), each with a mol. ion of m/z of 352.3 and MS2 fragments of 288.1, 305.2, 321.2 and 335.2. However, the intensities of the MS2 fragments were different among the two isomeric metabolites, and comparison to an authentic standard allowed for the structural determination of each metabolite. The isomeric metabolites M2A and M2B, resulting from amidoxime redns. of M1A and M1B, were also chromatog. separated and had distinguishable MS2 profiles that allowed for their structural assignments when compared to an authentic standard The di-amidoxime product resulting from O-demethylation of either side of DB844 was also identified as an abundant metabolite during microsomal incubations. The active antitrypanosomal metabolite, DB820, was the last metabolite to be formed and thus provides evidence that DB844 may effectively be metabolized to its active metabolite in vivo.

IT **619334-34-8**, DB 820 **619334-41-7**, DB 821
771534-68-0, DB 1058 **863015-96-7**
863015-97-8 863015-98-9 863016-43-7
863024-19-5, DB 1212
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro metabolism of orally active O-Me amidoxime prodrug DB844 for treatment of CNS trypanosomiasis)

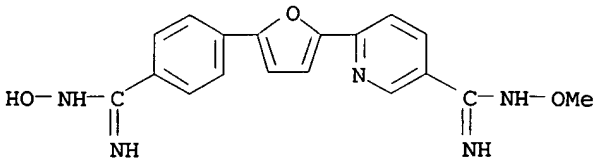
RN 619334-34-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



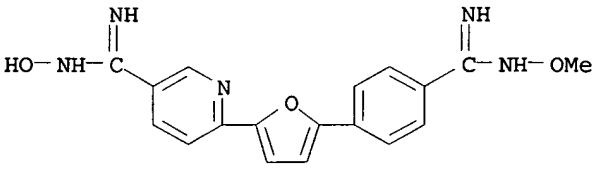
RN 619334-41-7 HCAPLUS
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



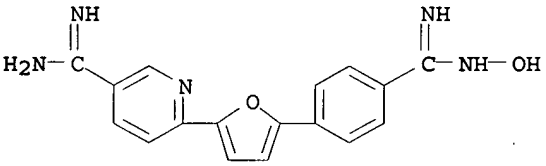
RN 771534-68-0 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[amino(hydroxyimino)methyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



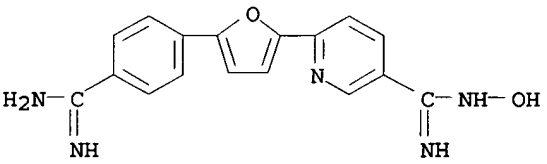
RN 863015-96-7 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[amino(methoxyimino)methyl]phenyl]-2-furanyl]-N-hydroxy- (9CI) (CA INDEX NAME)



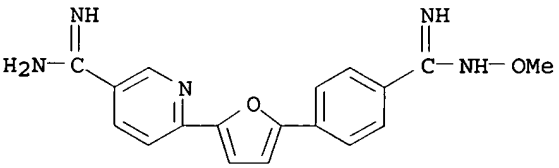
RN 863015-97-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[amino(hydroxyimino)methyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 863015-98-9 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-N-hydroxy- (9CI) (CA INDEX NAME)

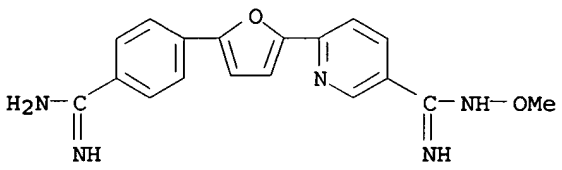


RN 863016-43-7 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[amino(methoxyimino)methyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)

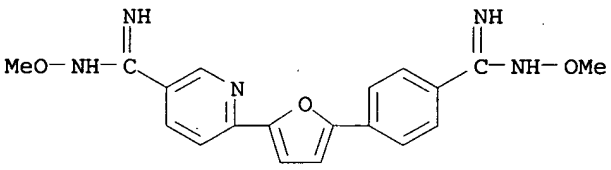


RN 863024-19-5 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-(aminoiminomethyl)phenyl]-2-

furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



IT **619334-44-0**, DB 844
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro metabolism of orally active O-Me amidoxime prodrug DB844 for treatment of CNS trypanosomiasis)
RN 619334-44-0 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



CC 1-2 (Pharmacology)
Section cross-reference(s): 63
IT 50864-64-7, NADPH cytochrome B5 reductase 330196-64-0, Cytochrome P 450 1A2 **619334-34-8**, DB 820
619334-41-7, DB 821 **771534-68-0**, DB 1058
863015-96-7 863015-97-8 863015-98-9
863016-43-7 863024-19-5, DB 1212
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro metabolism of orally active O-Me amidoxime prodrug DB844 for treatment of CNS trypanosomiasis)
IT **619334-44-0**, DB 844
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro metabolism of orally active O-Me amidoxime prodrug DB844 for treatment of CNS trypanosomiasis)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

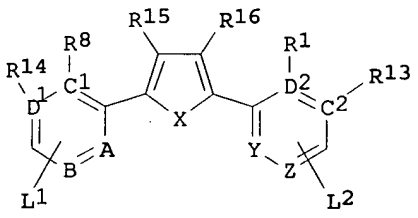
L35 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:490698 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 141:54198
TITLE: Preparation of dicationic 2,5-diarylfuran aza-analogs as anti-protozoan agents
INVENTOR(S): Boykin, David W.; Tidwell, Richard R.; Ismail, Mohamed A.; Brun, Reto
PATENT ASSIGNEE(S): University of North Carolina at Chapel Hill, USA; Georgia State University Research Foundation, Inc.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050018	A2	20040617	WO 2003-US37691	2003 1125
WO 2004050018	A3	20040708		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2504740	AA	20040617	CA 2003-2504740	2003 1125
US 2004122015	A1	20040624	US 2003-721525	2003 1125
EP 1565458	A2	20050824	EP 2003-787137	2003 1125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:	US 2002-429717P	P	2002 1127
	WO 2003-US37691	W	2003 1125

OTHER SOURCE(S): MARPAT 141:54198

GI



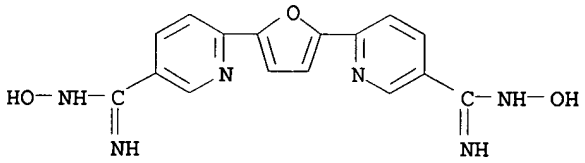
I

AB Heteroaryl diamidines and prodrugs thereof of formula (I) [L1 = C(:NR6)NR5R7, CH:NNHC(:NR6)NR5R7, NHC(:NR6)NR5R7; L2 = C(:NR3)NR2R4, CH:NNHC(:NR3)NR2R4, NHC(:NR3)NR2R4; X = O, S, NR17 (where R17 = H, lower alkyl); C1, C2, A, Y = CH, N, NR17, O, or S, wherein C1 and C2 are the same or different; D1, D2, B, Z = CH, N, or NR17, wherein D1 and D2 are the same or different; provided that B, Z, or both B and Z are not present when A, Y, or both A and Y are O, S, or NR17; R13,R14, R15, R16, R1, R8 = H, lower alkyl, halogen, alkoxy, aryloxy, aralkoxy, HO; R3, R6 = H, HO, lower alkyl, cycloalkyl, aryl, aralkyl, alkoxyl, hydroxycycloalkyl, alkoxycycloalkyl, hydroxyalkyl, aminoalkyl, acyloxy, AcO, alkylaminoalkyl; R2, R4, R5, R7 = H, lower alkyl,

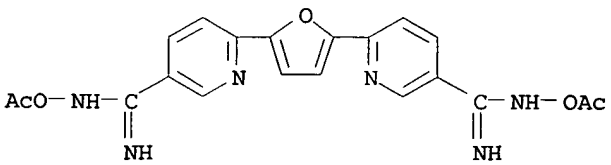
alkoxyalkyl, cycloalkyl, aryl, aralkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl; or R2 and R4 together or R5 and R7 together represent C2-10 alkyl, hydroxyalkyl, or alkylene, or R3 and R4 together or R6 and R7 together are (R9)n-substituted 1,2-phenylene (wherein n = 1-3; R9 = H, CONHR10NR11R12; wherein R10 = lower alkyl; R11, R12 = H, lower alkyl)] are prepared These compds. are useful for treating microbial infection, in particular a Trypanosoma brucei rhodesiense infection or a Plasmodium falciparum infection. Thus, Suzuki coupling of 4-cyanophenylboronic acid with 6-(5-bromofuran-2-yl)nicotinonitrile in the presence of tetrakis(triphenylphosphine)palladium in a mixture of toluene, MeOH, and 2 M aqueous Na2CO3 at 80° for 24 h to give 76% 6-[5-(4-cyanophenyl)furan-2-yl]nicotinonitrile which underwent addition reaction with hydroxylamine hydrochloride using potassium tert-butoxide in DMSO at room temperature overnight to give 91% N-hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine. O-methylation of the latter compound with di-Me sulfate in a mixture of dioxane and 2 N aqueous NaOH at 0-5° for 2 h gave N-methoxy-6-[5-[4-(N-methoxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine (II). Four compds. including 6-[5-(4-carbamimidoylphenyl)furan-2-yl]nicotinamidine (III) and its prodrug II show IC50 vs. P. falciparum at less than 10 ng/mL. III and its prodrug II cured the virulent STIB900 strain of T. brucei rhodesiense in a mouse model. In an experiment slated for 180 days, the prodrug II yielded parasite free mice in the CNS model through day 120 and thereby can be employed as an oral treatment of 2nd stage human African trypanosomiasis.

IT **619334-64-4P**, 2,5-Bis[5-(N-hydroxycarbamimidoyl)-2-pyridyl]furan **619334-66-6P**, 2,5-Bis[5-(N-acetoxycarbamimidoyl)-2-pyridyl]furan **619334-67-7P**, 2,5-Bis(5-amidino-2-pyridyl)furan **619334-76-8P**, 2,5-Bis[5-(N-methoxycarbamimidoyl)-2-pyridyl]furan **706785-01-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of dicationic 2,5-diarylfuran diamidines or prodrugs thereof as anti-protozoan agents)

RN 619334-64-4 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)

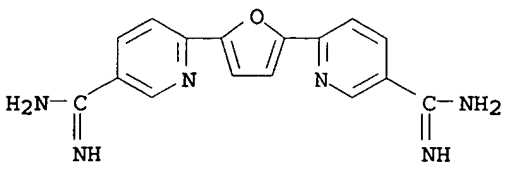


RN 619334-66-6 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis[N-(acetyloxy)- (9CI) (CA INDEX NAME)

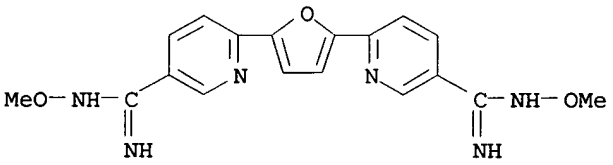


RN 619334-67-7 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis- (9CI) (CA

INDEX NAME)



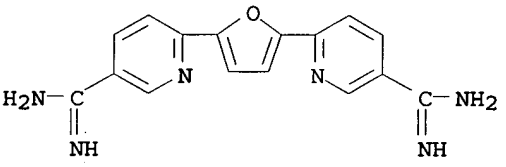
RN 619334-76-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



RN 706785-01-5 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis-, acetate (9CI) (CA INDEX NAME)

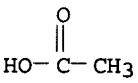
CM 1

CRN 619334-67-7
CMF C16 H14 N6 O



CM 2

CRN 64-19-7
CMF C2 H4 O2

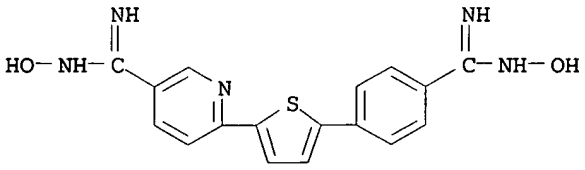


IT **619334-40-6P**, N-Hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)phenyl]thiophen-2-yl]nicotinamidine
619334-41-7P, N-Hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine
619334-54-2P, N-Hydroxy-5-[5-[4-(N-hydroxycarbamimidoyl)phenyl]furan-2-yl]pyridine-2-carboximidamide
706784-93-2P, N-Hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)-2-methylphenyl]furan-2-yl]nicotinamidine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of dicationic 2,5-diarylfuran diamidines or prodrugs

thereof as anti-protozoan agents)

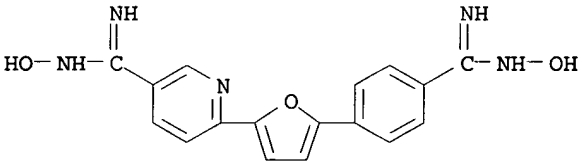
RN 619334-40-6 HCAPLUS

CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-thienyl]- (9CI) (CA INDEX NAME)



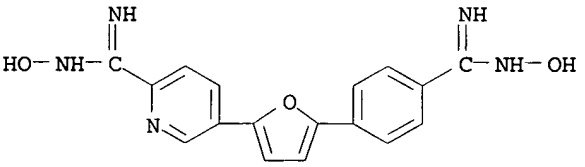
RN 619334-41-7 HCAPLUS

CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



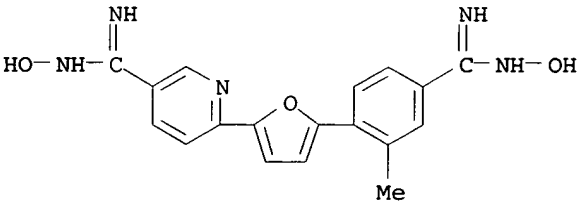
RN 619334-54-2 HCAPLUS

CN 2-Pyridinecarboximidamide, N-hydroxy-5-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 706784-93-2 HCAPLUS

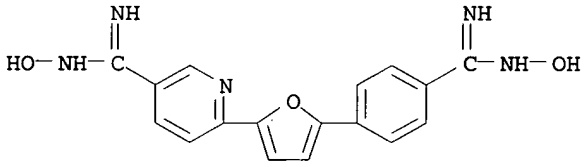
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]-2-methylphenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



IT **619334-31-5P**, N-Hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine trihydrochloride **619334-32-6P**, N-Methoxy-6-[5-[4-(N-methoxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine

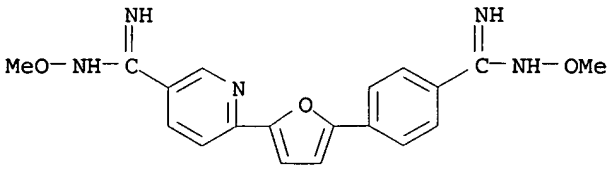
trihydrochloride **619334-33-7P**, N-Acetoxy-6-[5-[4-(N-Acetoxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine **619334-34-8P**, 6-[5-(4-Carbamimidoylphenyl)furan-2-yl]nicotinamidine **619334-35-9P**, 6-[5-(4-Carbamimidoylphenyl)furan-2-yl]nicotinamidine diacetate **619334-39-3P**, N-Hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)phenyl]thiophen-2-yl]nicotinamidine trihydrochloride **619334-42-8P**, N-Methoxy-6-[5-[4-(N-methoxycarbamimidoyl)phenyl]thiophen-2-yl]nicotinamidine trihydrochloride **619334-43-9P**, N-Methoxy-6-[5-[4-(N-methoxycarbamimidoyl)phenyl]thiophen-2-yl]nicotinamidine **619334-44-0P**, N-Methoxy-6-[5-[4-(N-methoxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine **619334-53-1P**, N-Hydroxy-5-[5-[4-(N-hydroxycarbamimidoyl)phenyl]furan-2-yl]pyridine-2-carboximidamide dihydrochloride **619334-55-3P**, N-Methoxy-5-[5-[4-(N-methoxycarbamimidoyl)phenyl]furan-2-yl]pyridine-2-carboximidamide **619334-59-7P**, N-Acetoxy-5-[5-[4-(N-Acetoxycarbamimidoyl)phenyl]furan-2-yl]pyridine-2-carboximidamide **619334-68-8P 619334-70-2P 619334-73-5P 619334-79-1P 706784-91-0P**, 5-[5-(4-Carbamimidoylphenyl)furan-2-yl]pyridine-2-carboximidamide acetate **706784-94-3P**, N-Acetoxy-6-[5-[4-(N-acetoxycarbamimidoyl)-2-methylphenyl]furan-2-yl]nicotinamidine **706784-96-5P**, 6-[5-(4-Carbamimidoyl-2-methylphenyl)furan-2-yl]nicotinamidine acetate **706785-00-4P 706785-02-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dicationic 2,5-diarylfuran diamidines or prodrugs thereof as anti-protozoan agents)

RN 619334-31-5 HCAPLUS
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-, trihydrochloride (9CI) (CA INDEX NAME)



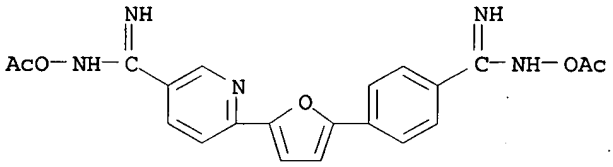
●3 HCl

RN 619334-32-6 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyimino)methyl]phenyl]-2-furanyl]-N-methoxy-, trihydrochloride (9CI) (CA INDEX NAME)

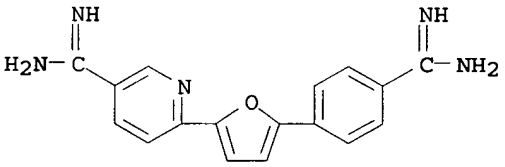


●3 HCl

RN 619334-33-7 HCAPLUS
CN 3-Pyridinecarboximidamide, N-(acetyloxy)-6-[5-[4-[[(acetyloxy)amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



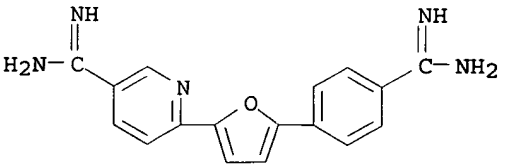
RN 619334-34-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 619334-35-9 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, diacetate (9CI) (CA INDEX NAME)

CM 1

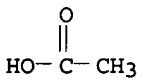
CRN 619334-34-8
CMF C17 H15 N5 O



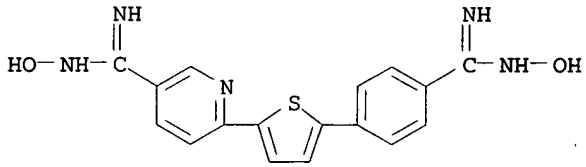
CM 2

CRN 64-19-7

CMF C2 H4 O2

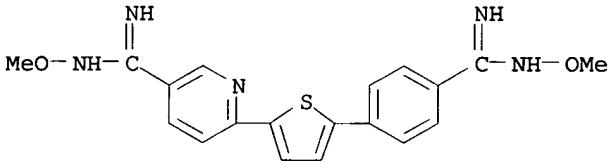


RN 619334-39-3 HCAPLUS
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-thienyl]-, trihydrochloride (9CI) (CA INDEX NAME)



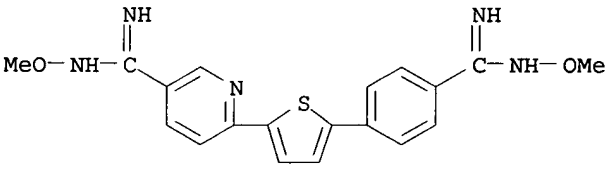
●3 HCl

RN 619334-42-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-thienyl]-N-methoxy-, trihydrochloride (9CI) (CA INDEX NAME)

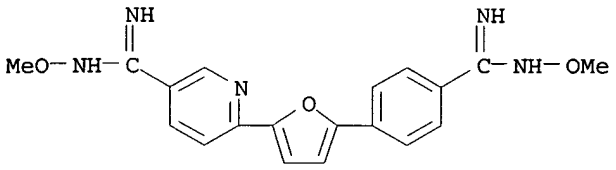


●3 HCl

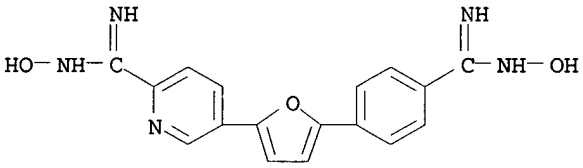
RN 619334-43-9 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-thienyl]-N-methoxy- (9CI) (CA INDEX NAME)



RN 619334-44-0 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)

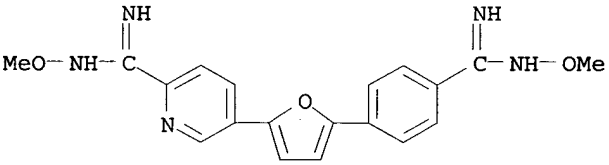


RN 619334-53-1 HCAPLUS
CN 2-Pyridinecarboximidamide, N-hydroxy-5-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)

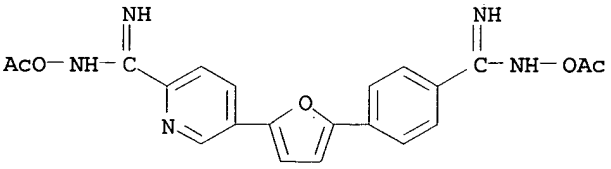


●2 HCl

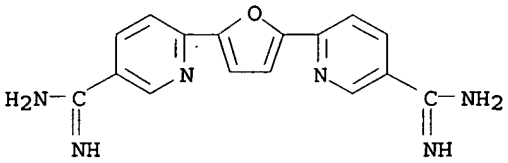
RN 619334-55-3 HCAPLUS
CN 2-Pyridinecarboximidamide, 5-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



RN 619334-59-7 HCAPLUS
CN 2-Pyridinecarboximidamide, N-(acetyloxy)-5-[5-[4-[[(acetyloxy)amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)

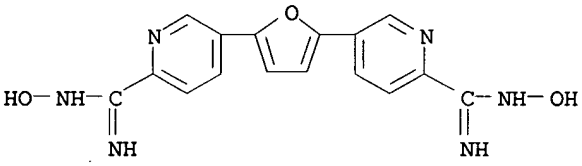


RN 619334-68-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis-, hydrochloride (10:33) (9CI) (CA INDEX NAME)

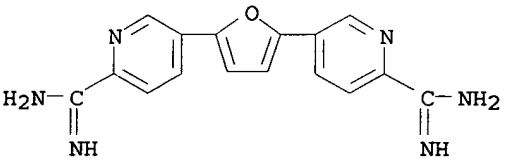


●33/10 HCl

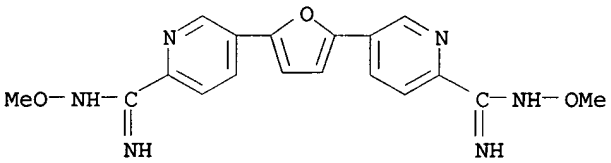
RN 619334-70-2 HCAPLUS
CN 2-Pyridinecarboximidamide, 5,5'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



RN 619334-73-5 HCAPLUS
CN 2-Pyridinecarboximidamide, 5,5'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



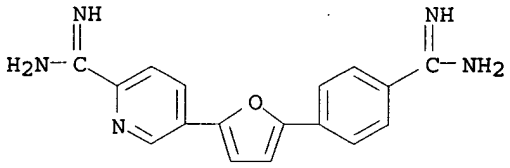
RN 619334-79-1 HCAPLUS
CN 2-Pyridinecarboximidamide, 5,5'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



RN 706784-91-0 HCAPLUS
CN 2-Pyridinecarboximidamide, 5-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, monoacetate (9CI) (CA INDEX NAME)

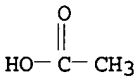
CM 1

CRN 619334-60-0
CMF C17 H15 N5 O

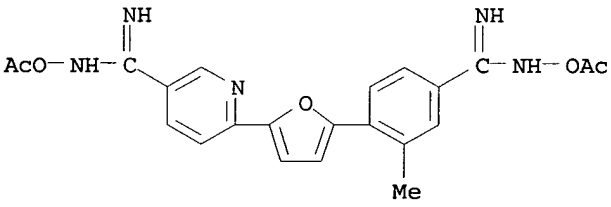


CM 2

CRN 64-19-7
CMF C2 H4 O2



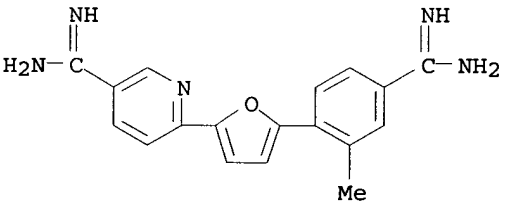
RN 706784-94-3 HCAPLUS
CN 3-Pyridinecarboximidamide, N-(acetyloxy)-6-[5-[4-[[(acetyloxy)amino]iminomethyl]-2-methylphenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 706784-96-5 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-(aminoiminomethyl)-2-methylphenyl]-2-furanyl]-, monoacetate (9CI) (CA INDEX NAME)

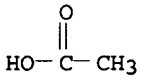
CM 1

CRN 706784-95-4
CMF C18 H17 N5 O

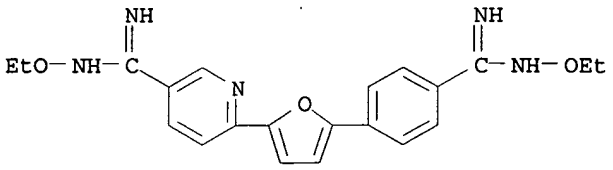


CM 2

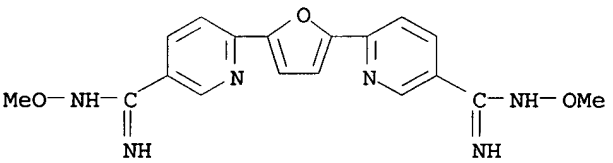
CRN 64-19-7
CMF C2 H4 O2



RN 706785-00-4 HCAPLUS
CN 3-Pyridinecarboximidamide, N-ethoxy-6-[5-[4-[(ethoxyamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 706785-02-6 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2-furandiyl)bis[N-methoxy-, hydrochloride (10:33) (9CI) (CA INDEX NAME)



●33/10 HCl

IC ICM A61K
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
IT 97483-77-7P, 5-Bromopyridine-2-carbonitrile 468068-39-5P, 6-Chloro-N-hydroxynicotinamidine 619334-29-1P, 6-(5-Bromofuran-2-yl)nicotinonitrile 619334-30-4P, 6-[5-(4-Cyanophenyl)furan-2-yl]nicotinonitrile 619334-36-0P, 6-(Thiophen-2-yl)nicotinonitrile 619334-37-1P, 6-(5-Bromothiophen-2-yl)nicotinonitrile 619334-38-2P, 6-[5-(4-Cyanophenyl)thiophen-2-yl]nicotinonitrile 619334-50-8P, 5-(Furan-2-yl)pyridine-2-carbonitrile 619334-51-9P, 5-(5-Bromofuran-2-yl)pyridine-2-carbonitrile 619334-52-0P, 5-[5-(4-Cyanophenyl)furan-2-yl]pyridine-2-carbonitrile 619334-62-2P, 2,5-Bis(5-cyano-2-pyridyl)furan **619334-64-4P**, 2,5-Bis[5-(N-hydroxycarbamimidoyl)-2-pyridyl]furan **619334-66-6P**, 2,5-Bis[5-(N-acetoxycarbamimidoyl)-2-pyridyl]furan **619334-67-7P**, 2,5-Bis(5-amidino-2-pyridyl)furan 619334-75-7P, 6-Chloro-N-methoxynicotinamidine **619334-76-8P**, 2,5-Bis[5-(N-methoxycarbamimidoyl)-2-pyridyl]furan 619334-81-5P, 6-[5-(4-Cyanobenzyl)furan-2-yl]nicotinonitrile 706784-92-1P, 6-[5-(4-Cyano-2-methylphenyl)furan-2-yl]nicotinonitrile 706784-97-6P, 6-(5-Styrylfuran-2-yl)nicotinonitrile **706785-01-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of dicationic 2,5-diarylfuran diamidines or prodrugs thereof as anti-protozoan agents)
IT **619334-40-6P**, N-Hydroxy-6-[5-[4-(N-

hydroxycarbamimidoyl)phenyl]thiophen-2-yl]nicotinamidine **619334-41-7P**, N-Hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine **619334-54-2P**, N-Hydroxy-5-[5-[4-(N-hydroxycarbamimidoyl)phenyl]furan-2-yl]pyridine-2-carboximidamide 619334-82-6P, N-Hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)benzyl]furan-2-yl]nicotinamidine **706784-93-2P**, N-Hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)-2-methylphenyl]furan-2-yl]nicotinamidine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of dicationic 2,5-diarylfuran diamidines or prodrugs thereof as anti-protozoan agents)

IT 6783-05-7P, (trans-2-Phenylvinyl)boronic acid **619334-31-5P**, N-Hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine trihydrochloride **619334-32-6P**, N-Methoxy-6-[5-[4-(N-methoxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine trihydrochloride **619334-33-7P**, N-Acetoxy-6-[5-[4-(N-Acetoxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine **619334-34-8P**, 6-[5-(4-Carbamimidoylphenyl)furan-2-yl]nicotinamidine **619334-35-9P**, 6-[5-(4-Carbamimidoylphenyl)furan-2-yl]nicotinamidine diacetate **619334-39-3P**, N-Hydroxy-6-[5-[4-(N-hydroxycarbamimidoyl)phenyl]thiophen-2-yl]nicotinamidine trihydrochloride **619334-42-8P**, N-Methoxy-6-[5-[4-(N-methoxycarbamimidoyl)phenyl]thiophen-2-yl]nicotinamidine trihydrochloride **619334-43-9P**, N-Methoxy-6-[5-[4-(N-methoxycarbamimidoyl)phenyl]thiophen-2-yl]nicotinamidine **619334-44-0P**, N-Methoxy-6-[5-[4-(N-methoxycarbamimidoyl)phenyl]furan-2-yl]nicotinamidine **619334-53-1P**, N-Hydroxy-5-[5-[4-(N-hydroxycarbamimidoyl)phenyl]furan-2-yl]pyridine-2-carboximidamide dihydrochloride **619334-55-3P**, N-Methoxy-5-[5-[4-(N-methoxycarbamimidoyl)phenyl]furan-2-yl]pyridine-2-carboximidamide **619334-59-7P**, N-Acetoxy-5-[5-[4-(N-Acetoxycarbamimidoyl)phenyl]furan-2-yl]pyridine-2-carboximidamide **619334-68-8P 619334-70-2P 619334-73-5P** **619334-79-1P** 619334-83-7P, N-Acetoxy-6-[5-[4-(N-acetoxycarbamimidoyl)benzyl]furan-2-yl]nicotinamidine 619334-85-9P, 6-[5-(4-Carbamimidoylbenzyl)furan-2-yl]nicotinamidine diacetate **706784-91-0P**, 5-[5-(4-Carbamimidoylphenyl)furan-2-yl]pyridine-2-carboximidamide acetate **706784-94-3P**, N-Acetoxy-6-[5-[4-(N-acetoxycarbamimidoyl)-2-methylphenyl]furan-2-yl]nicotinamidine **706784-96-5P**, 6-[5-(4-Carbamimidoyl-2-methylphenyl)furan-2-yl]nicotinamidine acetate 706784-98-7P, N-Hydroxy-6-(5-styrylfuran-2-yl)nicotinamidine 706784-99-8P, N-Hydroxy-6-(5-styrylfuran-2-yl)nicotinamidine dihydrochloride **706785-00-4P 706785-02-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dicationic 2,5-diarylfuran diamidines or prodrugs thereof as anti-protozoan agents)

L35 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:396314 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 141:332021
TITLE: Synthesis of deuterium-labelled 6-[5-(4-amidinophenyl)furan-2-yl]nicotinamidine and N-alkoxy-6-{5-[4-(N-alkoxyamidino)phenyl]furan-2-yl}nicotinamidines
AUTHOR(S): Ismail, Mohamed A.; Boykin, David W.
CORPORATE SOURCE: Department of Chemistry, Georgia State

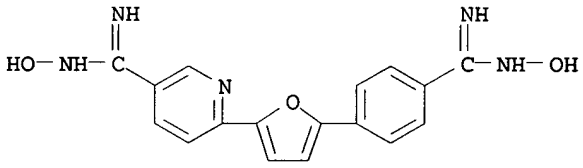
University, Atlanta, GA, 30303, USA
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (2004), 47(4), 233-242
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 6-[5-(4-Amidinophenyl)furan-2-yl]nicotinamidine-d4 (5) was synthesized from 6-[5-(4-cyanophenyl)furan-2-yl]nicotinonitrile-d4 (3), through the bis-O-acetoxy-amidoxime followed by hydrogenation. Compound 3 was prepared from 6-(furan-2-yl)nicotinonitrile by a Heck coupling reaction with 4-bromobenzonitrile-d4, a product of selective cyanation reaction of 1,4-dibromobenzene-d4 with CuCN. D-labeled N-methoxy-6-[5-[4-(N-methoxyamidino)phenyl]furan-2-yl]nicotinamidines were prepared via methylation of their resp. amidoximes with di-Me sulfate-d6 in aqueous NaOH in good yields.

IT **619334-41-7**, N-Hydroxy-6-[5-[4-(N-hydroxyamidino)phenyl]furan-2-yl]nicotinamidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of deuterium-labeled [(amidinophenyl)furanyl]nicotinamidine and N-alkoxy-[[(N-alkoxyamidino)phenyl]furanyl]nicotinamidine prodrugs)

RN 619334-41-7 HCAPLUS

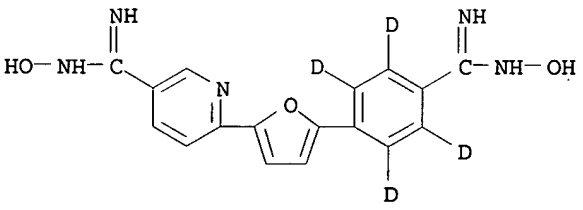
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



IT **771534-58-8P 771534-64-6P 771534-68-0P**
, 6-[5-[4-(N-Hydroxyamidino)phenyl]furan-2-yl]-N-methoxynicotinamidine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of deuterium-labeled [(amidinophenyl)furanyl]nicotinamidine and N-alkoxy-[[(N-alkoxyamidino)phenyl]furanyl]nicotinamidine prodrugs)

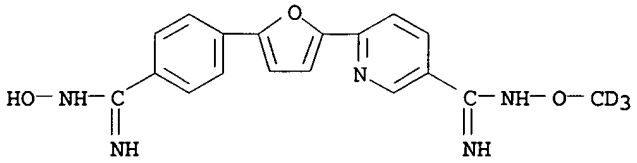
RN 771534-58-8 HCAPLUS

CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl-2,3,5,6-d4]-2-furanyl]- (9CI) (CA INDEX NAME)

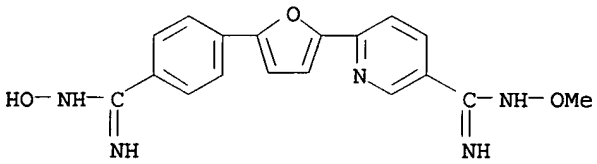


RN 771534-64-6 HCAPLUS

CN 3-Pyridinecarboximidamide, 6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-(methoxy-d3)- (9CI) (CA INDEX NAME)



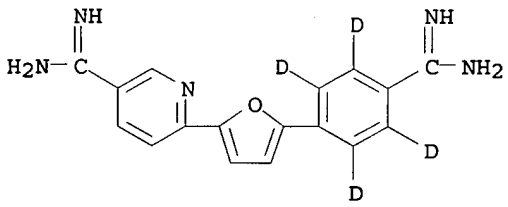
RN 771534-68-0 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[amino(hydroxyimino)methyl]phen
yl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



IT **771534-60-2P 771534-65-7P 771534-69-1P**
771534-70-4P 771534-71-5P 771534-72-6P
771534-73-7P 771534-74-8P 771534-75-9P
771534-76-0P 771534-77-1P 771534-78-2P
, 6-[5-[4-(N-Hydroxyamidino)phenyl]furan-2-yl]-N-
methoxynicotinamidine trihydrochloride **771534-79-3P**
771534-80-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of deuterium-labeled [(amidinophenyl)furanyl]nicotin
amidine and N-alkoxy-[[(N-alkoxyamidino)phenyl]furanyl]nicotina
midine prodrugs)
RN 771534-60-2 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-(aminoiminomethyl)phenyl-
2,3,5,6-d4]-2-furanyl]-, diacetate (9CI) (CA INDEX NAME)

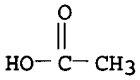
CM 1

CRN 771534-59-9
CMF C17 H11 D4 N5 O



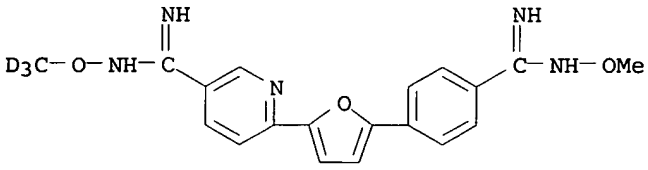
CM 2

CRN 64-19-7
CMF C2 H4 O2

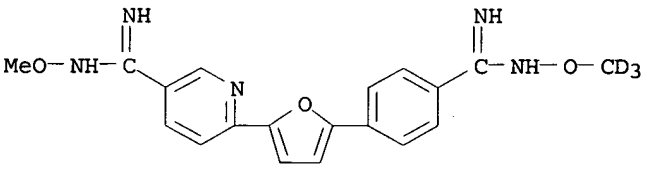


RN 771534-65-7 HCAPLUS

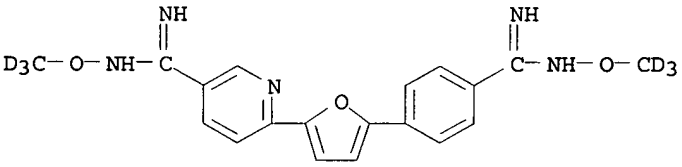
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phen
yl]-2-furanyl]-N-(methoxy-d3)- (9CI) (CA INDEX NAME)



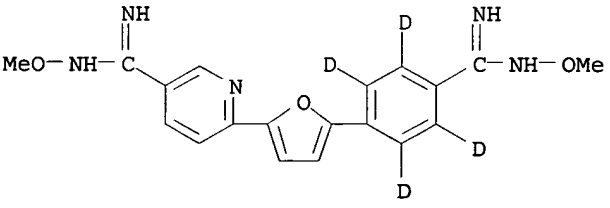
RN 771534-69-1 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxy-d3-
amino)methyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



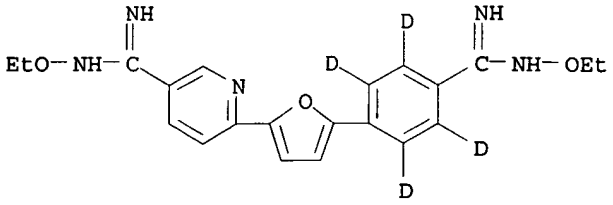
RN 771534-70-4 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxy-d3-
amino)methyl]phenyl]-2-furanyl]-N-(methoxy-d3)- (9CI) (CA INDEX
NAME)



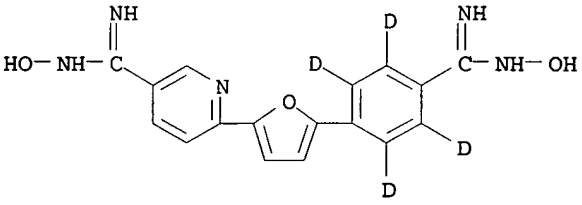
RN 771534-71-5 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phen
yl-2,3,5,6-d4]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



RN 771534-72-6 HCAPLUS
CN 3-Pyridinecarboximidamide, N-ethoxy-6-[5-[4-
[(ethoxyamino)iminomethyl]phenyl-2,3,5,6-d4]-2-furanyl]- (9CI)
(CA INDEX NAME)

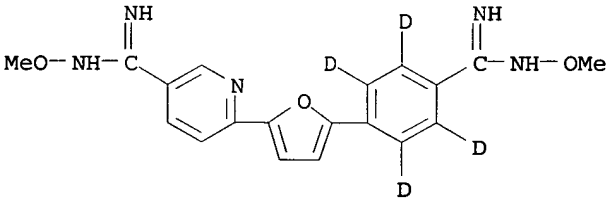


RN 771534-73-7 HCAPLUS
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl-2,3,5,6-d4]-2-furanyl]-, trihydrochloride (9CI) (CA INDEX NAME)



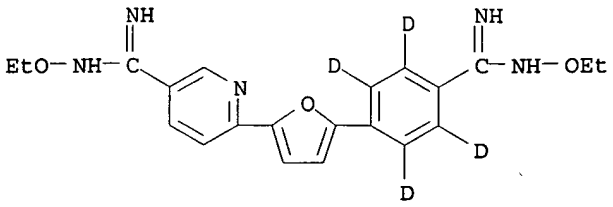
●3 HCl

RN 771534-74-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phenyl-2,3,5,6-d4]-2-furanyl]-N-methoxy-, trihydrochloride (9CI) (CA INDEX NAME)



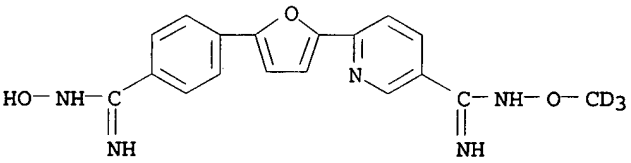
●3 HCl

RN 771534-75-9 HCAPLUS
CN 3-Pyridinecarboximidamide, N-ethoxy-6-[5-[4-[(ethoxyamino)iminomethyl]phenyl-2,3,5,6-d4]-2-furanyl]-, trihydrochloride (9CI) (CA INDEX NAME)



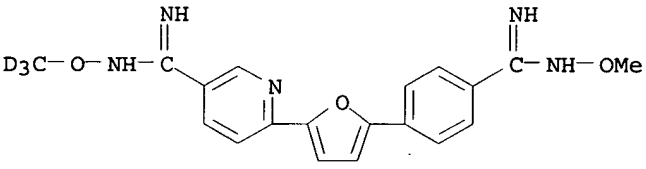
●3 HCl

RN 771534-76-0 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-(methoxy-d3)-, trihydrochloride (9CI) (CA INDEX NAME)



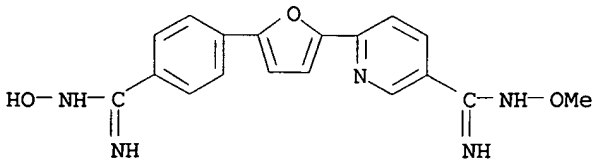
●3 HCl

RN 771534-77-1 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-furanyl]-N-(methoxy-d3)-, trihydrochloride (9CI) (CA INDEX NAME)



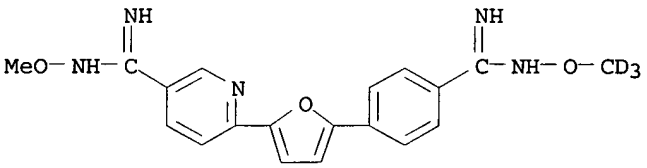
●3 HCl

RN 771534-78-2 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[amino(hydroxyimino)methyl]phenyl]-2-furanyl]-N-methoxy-, trihydrochloride (9CI) (CA INDEX NAME)



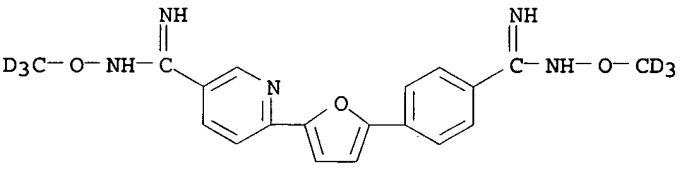
●3 HCl

RN 771534-79-3 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxy-d3-amino)methyl]phenyl]-2-furanyl]-N-methoxy-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

RN 771534-80-6 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxy-d3-amino)methyl]phenyl]-2-furanyl]-N-(methoxy-d3)-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
IT 126747-14-6, 4-Cyanophenylboronic acid 619334-29-1, 6-(5-Bromofuran-2-yl)nicotinonitrile **619334-41-7**, N-Hydroxy-6-[5-[4-(N-hydroxyamidino)phenyl]furan-2-yl]nicotinamidine 771534-56-6, 4-Bromobenzonitrile-d4
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of deuterium-labeled [(amidinophenyl)furanyl]nicotinamidine and N-alkoxy-[[(N-alkoxyamidino)phenyl]furanyl]nicotinamidine prodrugs)
IT 771534-57-7P **771534-58-8P** 771534-61-3P, 6-(5-Bromofuran-2-yl)-N-hydroxynicotinamidine 771534-63-5P **771534-64-6P** 771534-66-8P, 6-(5-Bromofuran-2-yl)-N-methoxynicotinamidine 771534-67-9P, 6-[5-(4-Cyanophenyl)furan-2-yl]-N-methoxynicotinamidine **771534-68-0P**,

6-[5-[4-(N-Hydroxyamidino)phenyl]furan-2-yl]-N-methoxynicotinamidine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of deuterium-labeled [(amidinophenyl)furanyl]nicotinamidine and N-alkoxy-[[(N-alkoxyamidino)phenyl]furanyl]nicotinamidine prodrugs)

IT **771534-60-2P 771534-65-7P 771534-69-1P**
771534-70-4P 771534-71-5P 771534-72-6P
771534-73-7P 771534-74-8P 771534-75-9P
771534-76-0P 771534-77-1P 771534-78-2P
, 6-[5-[4-(N-Hydroxyamidino)phenyl]furan-2-yl]-N-methoxynicotinamidine trihydrochloride **771534-79-3P**
771534-80-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of deuterium-labeled [(amidinophenyl)furanyl]nicotinamidine and N-alkoxy-[[(N-alkoxyamidino)phenyl]furanyl]nicotinamidine prodrugs)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:758932 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 139:364780
TITLE: Synthesis and Antiprotozoal Activity of Aza-Analogues of Furamidine
AUTHOR(S): Ismail, Mohamed A.; Brun, Reto; Easterbrook, Judy D.; Tanious, Farial A.; Wilson, W. David; Boykin, David W.
CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303-3083, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(22), 4761-4769
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:364780
GI

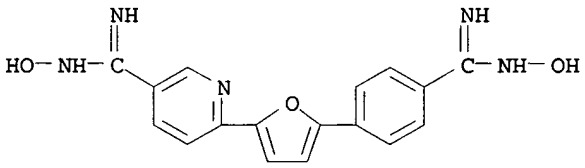
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 6-[5-(4-Amidinophenyl)furan-2-yl]nicotinamidine (I; X = O, R = H) was synthesized from 6-[5-(4-cyanophenyl)furan-2-yl]nicotinonitrile (II), through the bis-O-acetoxyamidoxime followed by hydrogenation. Compound II was prepared via selective bromination of 6-(furan-2-yl)nicotinonitrile with N-bromosuccinimide, followed by Suzuki coupling with 4-cyanophenylboronic acid. In a similar way, diamidines III and IV (R = H) were prepared from the corresponding dicyano derivs. N-Methoxy-6-{5-[4-(N-methoxyamidino)phenyl]-furan-2-yl}-nicotinamidine (I; X = O, R = OMe) was prepared via methylation of the resp. diamidoxime with dimethylsulfate. Prodrugs I (X = S, R = OMe) and IV (R = OMe) were also prepared by methylation of the resp. diamidoximes. The sym. diamidines V and VI were synthesized through the corresponding bis-O-acetoxyamidoxime followed by hydrogenation. The corresponding dicyano precursors were conveniently obtained by Stille coupling between 2,5-bis(tri-n-butylstannyl)furan and the corresponding heteroaryl halides. These compds. have been evaluated in vitro for activity against Trypanosoma b. rhodesiense (T. b. r.) and P. falciparum

(P. f.). The diamidines I (X = O, R = H) and IV (R = H), and VI gave IC50 values vs. T. b. r. of less than 10 nM. Against P. f. I (X = O, R = H) and III, and VI exhibited IC50 values less than 10 nM. In an in vivo mouse model for T. b. r. compds. I (X = O, R = OMe, OEt, and H) and IV (R = OMe) were curative. I (X = O, R = OMe) produced cures at an oral dosage of 5 mg/kg.

IT **619334-31-5P 619334-35-9P 619334-39-3P**
619334-40-6P 619334-41-7P 619334-43-9P
619334-44-0P 619334-45-1P 619334-53-1P
619334-54-2P 619334-55-3P 619334-57-5P
619334-63-3P 619334-64-4P 619334-67-7P
619334-70-2P 619334-71-3P 619334-76-8P
619334-79-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation, DNA binding affinity, trypanocidal and antimalarial activity of furamidine aza analogs)

RN 619334-31-5 HCAPLUS
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-, trihydrochloride (9CI) (CA INDEX NAME)

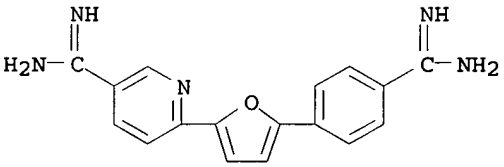


●3 HCl

RN 619334-35-9 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, diacetate (9CI) (CA INDEX NAME)

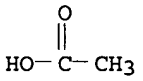
CM 1

CRN 619334-34-8
CMF C17 H15 N5 O

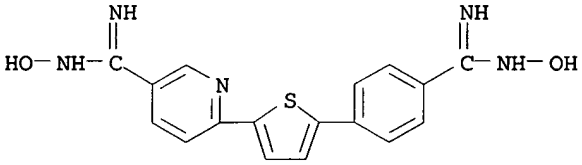


CM 2

CRN 64-19-7
CMF C2 H4 O2

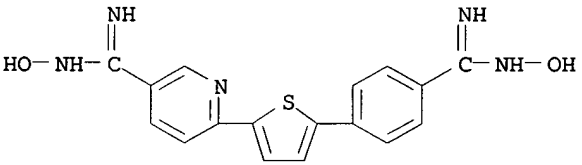


RN 619334-39-3 HCAPLUS
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-thienyl]-, trihydrochloride (9CI) (CA INDEX NAME)

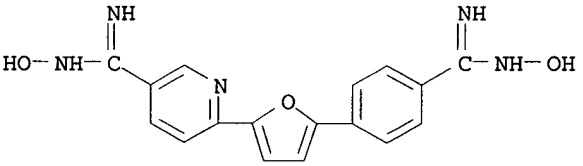


●3 HCl

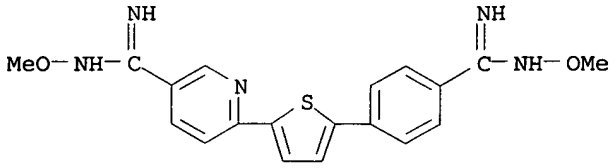
RN 619334-40-6 HCAPLUS
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-thienyl]- (9CI) (CA INDEX NAME)



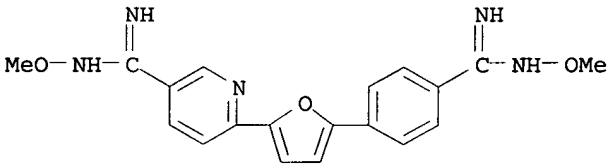
RN 619334-41-7 HCAPLUS
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



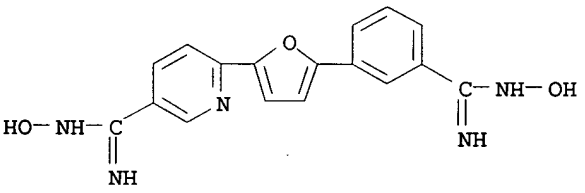
RN 619334-43-9 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-thienyl]-N-methoxy- (9CI) (CA INDEX NAME)



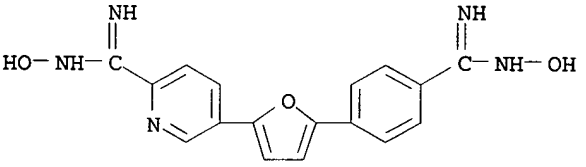
RN 619334-44-0 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



RN 619334-45-1 HCAPLUS
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[3-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)

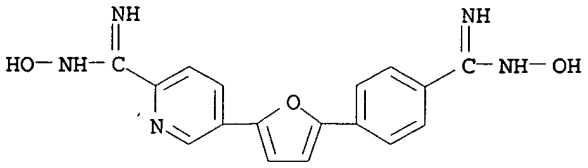


RN 619334-53-1 HCAPLUS
CN 2-Pyridinecarboximidamide, N-hydroxy-5-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)

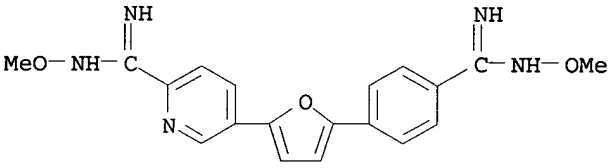


●2 HCl

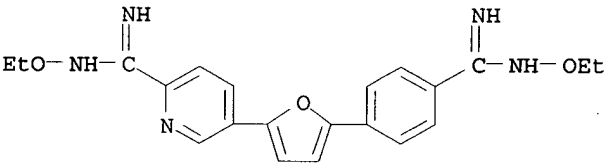
RN 619334-54-2 HCAPLUS
CN 2-Pyridinecarboximidamide, N-hydroxy-5-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



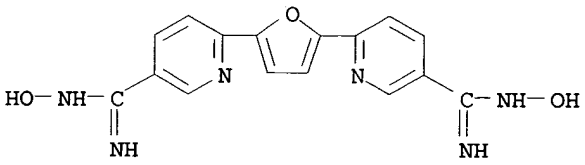
RN 619334-55-3 HCAPLUS
CN 2-Pyridinecarboximidamide, 5-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



RN 619334-57-5 HCAPLUS
CN 2-Pyridinecarboximidamide, N-ethoxy-5-[5-[4-[(ethoxyamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)

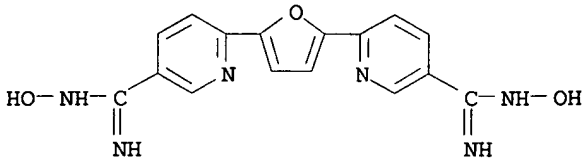


RN 619334-63-3 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis[N-hydroxy-, hydrochloride (20:63) (9CI) (CA INDEX NAME)

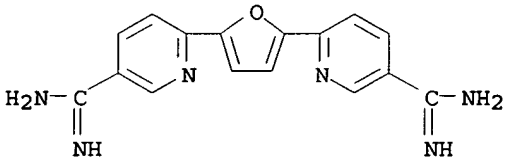


●63/20 HCl

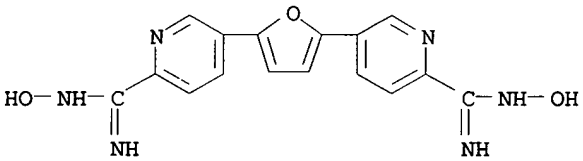
RN 619334-64-4 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



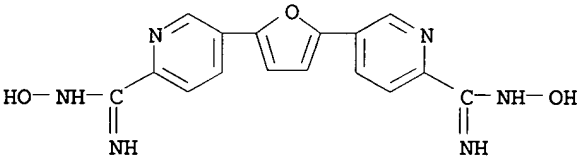
RN 619334-67-7 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 619334-70-2 HCAPLUS
CN 2-Pyridinecarboximidamide, 5,5'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)

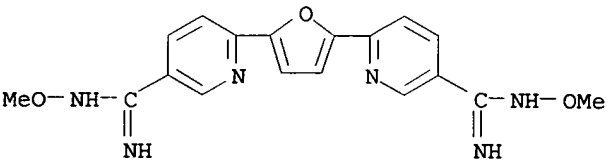


RN 619334-71-3 HCAPLUS
CN 2-Pyridinecarboximidamide, 5,5'-(2,5-furandiyl)bis[N-hydroxy-, dihydrochloride (9CI) (CA INDEX NAME)



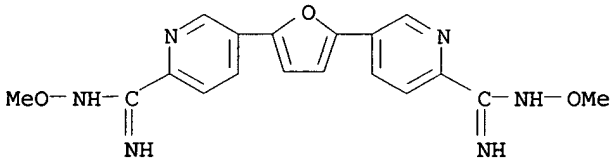
●2 HCl

RN 619334-76-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



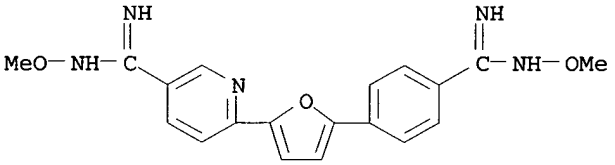
RN 619334-79-1 HCAPLUS

CN 2-Pyridinecarboximidamide, 5,5'-(2,5-furandiyl)bis[N-methoxy-
(9CI) (CA INDEX NAME)



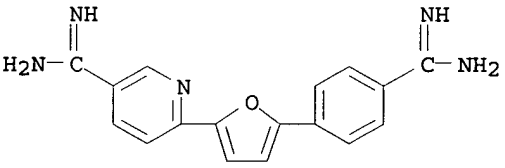
IT **619334-32-6P 619334-34-8P 619334-42-8P**
619334-49-5P 619334-56-4P 619334-58-6P
619334-61-1P 619334-68-8P 619334-74-6P
619334-77-9P 619334-80-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
BIOL (Biological study); PREP (Preparation)
(preparation, DNA binding affinity, trypanocidal and antimalarial
activity of furamidine aza analogs)

RN 619334-32-6 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyimino)methyl]phen
yl]-2-furanyl]-N-methoxy-, trihydrochloride (9CI) (CA INDEX NAME)

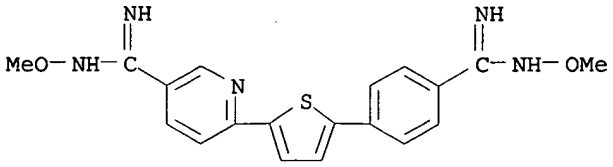


●3 HCl

RN 619334-34-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-(aminoiminomethyl)phenyl]-2-
furanyl]- (9CI) (CA INDEX NAME)



RN 619334-42-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[4-[imino(methoxyamino)methyl]phen
yl]-2-thienyl]-N-methoxy-, trihydrochloride (9CI) (CA INDEX NAME)

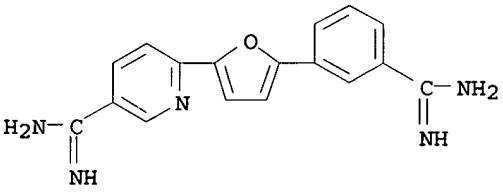


●3 HCl

RN 619334-49-5 HCAPLUS
CN 3-Pyridinecarboximidamide, 6-[5-[3-(aminoiminomethyl)phenyl]-2-furanyl]-, diacetate (9CI) (CA INDEX NAME)

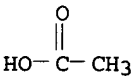
CM 1

CRN 619334-48-4
CMF C17 H15 N5 O

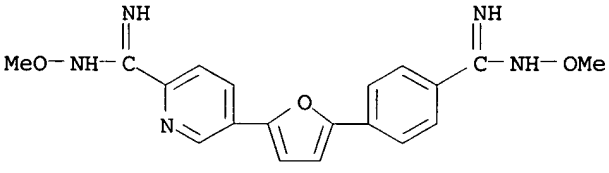


CM 2

CRN 64-19-7
CMF C2 H4 O2



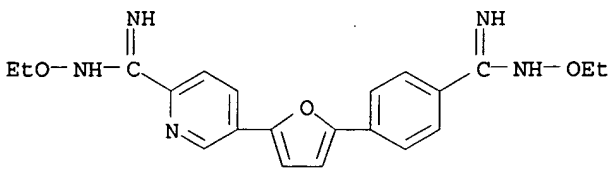
RN 619334-56-4 HCAPLUS
CN 2-Pyridinecarboximidamide, 5-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-furanyl]-N-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 619334-58-6 HCAPLUS
CN 2-Pyridinecarboximidamide, N-ethoxy-5-[5-[4-[(ethoxyamino)iminomethyl]phenyl]-2-furanyl]-, trihydrochloride

(9CI) (CA INDEX NAME)

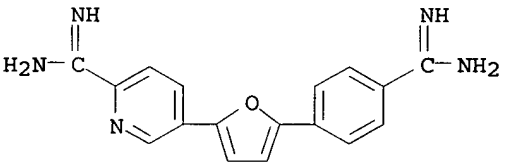


●3 HCl

RN 619334-61-1 HCAPLUS
CN 2-Pyridinecarboximidamide, 5-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, triacetate (9CI) (CA INDEX NAME)

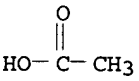
CM 1

CRN 619334-60-0
CMF C17 H15 N5 O

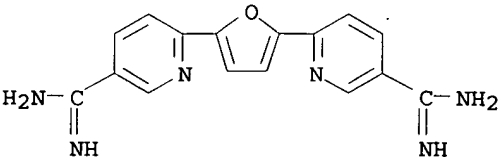


CM 2

CRN 64-19-7
CMF C2 H4 O2



RN 619334-68-8 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis-, hydrochloride (10:33) (9CI) (CA INDEX NAME)



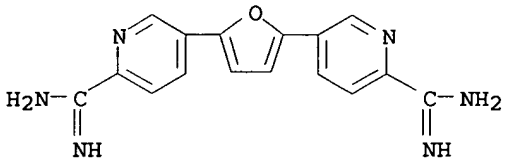
●33/10 HCl

RN 619334-74-6 HCAPLUS
CN 2-Pyridinecarboximidamide, 5,5'-(2,5-furandiyl)bis-, diacetate

(9CI) (CA INDEX NAME)

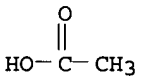
CM 1

CRN 619334-73-5
CMF C16 H14 N6 O

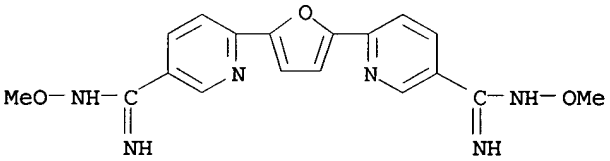


CM 2

CRN 64-19-7
CMF C2 H4 O2

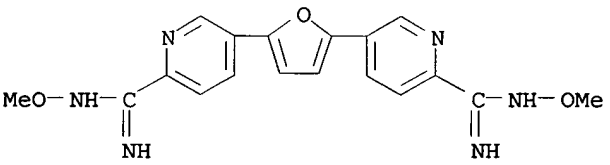


RN 619334-77-9 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis[N-methoxy-, hydrochloride (4:13) (9CI) (CA INDEX NAME)



●13/4 HCl

RN 619334-80-4 HCAPLUS
CN 2-Pyridinecarboximidamide, 5,5'-(2,5-furandiyl)bis[N-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)

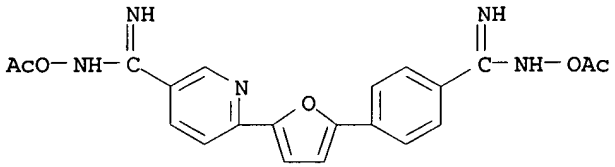


●2 HCl

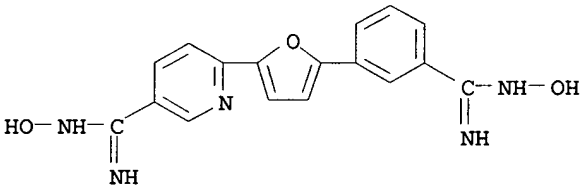
IT **619334-33-7P 619334-46-2P 619334-47-3P**
619334-59-7P 619334-66-6P 619334-72-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, DNA binding affinity, trypanocidal and antimalarial activity of furamidine aza analogs)

RN 619334-33-7 HCAPLUS
CN 3-Pyridinecarboximidamide, N-(acetyloxy)-6-[5-[4-[[(acetyloxy)amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)

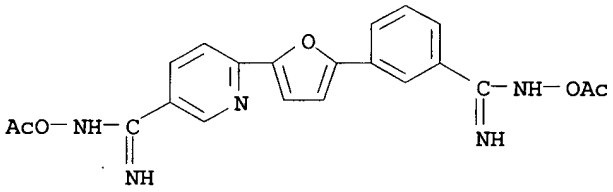


RN 619334-46-2 HCAPLUS
CN 3-Pyridinecarboximidamide, N-hydroxy-6-[5-[3-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-, trihydrochloride (9CI) (CA INDEX NAME)

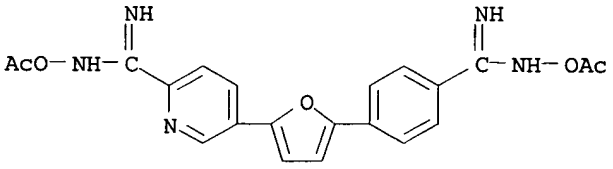


●3 HCl

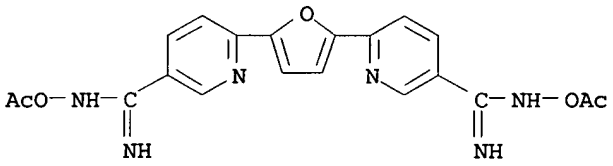
RN 619334-47-3 HCAPLUS
CN 3-Pyridinecarboximidamide, N-(acetyloxy)-6-[5-[3-[[(acetyloxy)amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



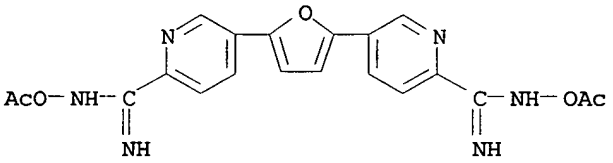
RN 619334-59-7 HCAPLUS
CN 2-Pyridinecarboximidamide, N-(acetyloxy)-5-[5-[4-[[(acetyloxy)amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 619334-66-6 HCAPLUS
CN 3-Pyridinecarboximidamide, 6,6'-(2,5-furandiyl)bis[N-(acetyloxy)-
(9CI) (CA INDEX NAME)



RN 619334-72-4 HCAPLUS
CN 2-Pyridinecarboximidamide, 5,5'-(2,5-furandiyl)bis[N-(acetyloxy)-
(9CI) (CA INDEX NAME)



CC 27-6 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 10
IT **619334-31-5P 619334-35-9P 619334-39-3P**
619334-40-6P 619334-41-7P 619334-43-9P
619334-44-0P 619334-45-1P 619334-53-1P
619334-54-2P 619334-55-3P 619334-57-5P
619334-63-3P 619334-64-4P 619334-67-7P
619334-70-2P 619334-71-3P 619334-76-8P
619334-79-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation, DNA binding affinity, trypanocidal and antimalarial activity of furamidine aza analogs)
IT **619334-32-6P 619334-34-8P 619334-42-8P**
619334-49-5P 619334-56-4P 619334-58-6P
619334-61-1P 619334-68-8P 619334-74-6P
619334-77-9P 619334-80-4P 619334-85-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, DNA binding affinity, trypanocidal and antimalarial activity of furamidine aza analogs)
IT 97483-77-7P, 5-Bromopyridine-2-carbonitrile 380380-62-1P
453568-68-8P 468068-39-5P 619334-28-0P 619334-29-1P
619334-30-4P **619334-33-7P** 619334-36-0P 619334-37-1P
619334-38-2P **619334-46-2P 619334-47-3P**
619334-50-8P 619334-51-9P 619334-52-0P **619334-59-7P**
619334-62-2P **619334-66-6P** 619334-69-9P
619334-72-4P 619334-75-7P 619334-78-0P 619334-81-5P
619334-82-6P 619334-83-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, DNA binding affinity, trypanocidal and antimalarial activity of furamidine aza analogs)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:496856 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 140:59488
TITLE: Heck arylation of cyclic enol ethers with aryldiazonium salts: regio- and stereoselective synthesis of arylated oxacycles
AUTHOR(S): Schmidt, Bernd
CORPORATE SOURCE: Universitaet Dortmund, Fachbereich Chemie - Organische Chemie, Dortmund, D-44227, Germany
SOURCE: Chemical Communications (Cambridge, United Kingdom) (2003), (14), 1656-1657
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:59488
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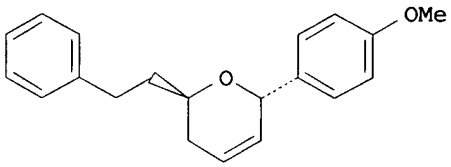


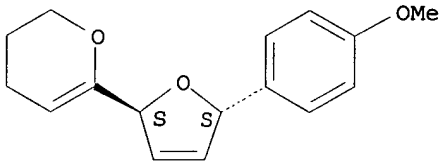
I

AB Dihydropyrans, e.g., I, and dihydrofurans bearing an aryl substituent in the 2-position were regio- and stereoselectively synthesized by Heck arylation of cyclic enol ethers with aryldiazonium salts.

IT **695183-33-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(regio- and stereoselective preparation of methoxyphenyldihydropyrans and -furans via Heck arylation of dihydropyrans and -furans with methoxyphenyldiazonium tetrafluoroborate)

RN 695183-33-6 HCAPLUS
CN 2H-Pyran, 6-[(2S,5S)-2,5-dihydro-5-(4-methoxyphenyl)-2-furanyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 27-13 (Heterocyclic Compounds (One Hetero Atom))
IT 400884-76-6P 637332-61-7P 637332-62-8P 637334-43-1P 637334-44-2P **695183-33-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(regio- and stereoselective preparation of methoxyphenyldihydropyrans and -furans via Heck arylation of dihydropyrans and -furans with methoxyphenyldiazonium tetrafluoroborate)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:249167 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 137:106164
TITLE: Botryolins A and B, two tetramethylsqualene triethers from the green microalga Botryococcus braunii
AUTHOR(S): Metzger, Pierre; Rager, Marie-Noelle; Largeau, Claude
CORPORATE SOURCE: Laboratoire de Chimie Bioorganique et Organique Physique, Ecole Nationale Superieure de Chimie de Paris, UMR CNRS 7573, Paris, 75231, Fr.
SOURCE: Phytochemistry (2002), 59(8), 839-843
CODEN: PYTCAS; ISSN: 0031-9422
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
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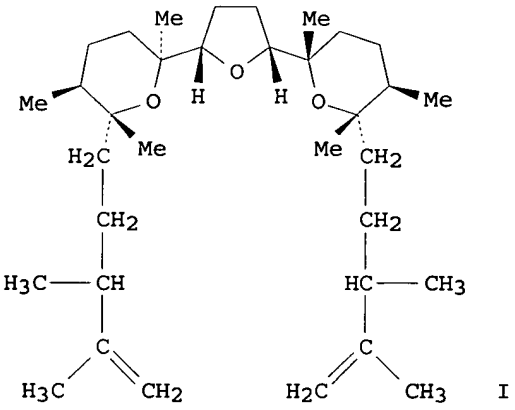


I

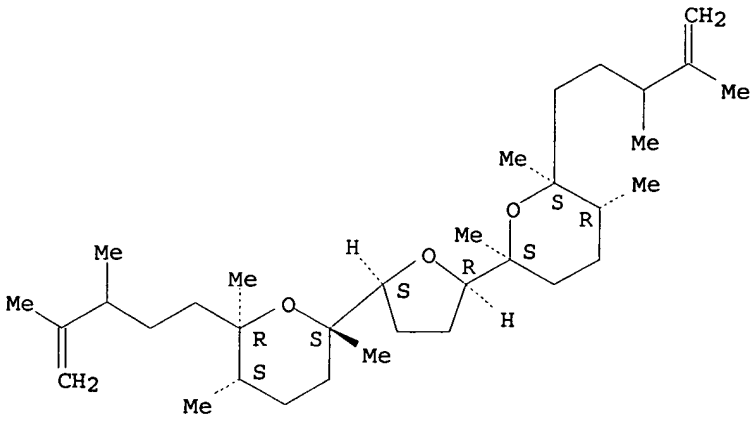
AB Two new triterpenoid polyethers with a tetramethylsqualene carbon skeleton, botryolins A (I) and B, have been isolated from the green microalga Botryococcus braunii. Their structures were determined by means of spectral analyses including 2D NMR.

IT **443782-82-9P**, Botryolin A **443782-83-0P**, Botryolin B
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(triterpenoid polyethers botryolin A and botryolin B from green microalga Botryococcus)

RN 443782-82-9 HCAPLUS

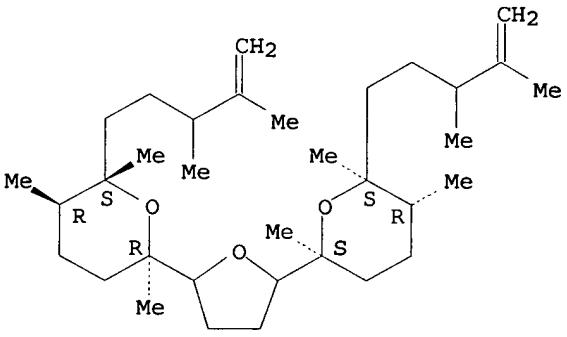
CN 2H-Pyran, 2,2'-[(2R,5S)-tetrahydro-2,5-furandiyl]bis[6-(3,4-dimethyl-4-pentenyl)tetrahydro-2,5,6-trimethyl-, (2S,2'S,5R,5'S,6S,6'R)-rel- (9CI) (CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown.
Currently available stereo shown.



RN 443782-83-0 HCAPLUS
CN 2H-Pyran, 2,2'-(tetrahydro-2,5-furandiyl)bis[6-(3,4-dimethyl-4-pentenyl)tetrahydro-2,5,6-trimethyl-, (2R,2'R,5R,5'R,6S,6'S)-rel-(9CI) (CA INDEX NAME)

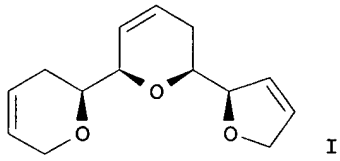
Rotation (-). Absolute stereochemistry unknown.
Currently available stereo shown.



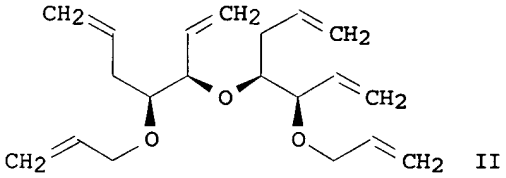
CC 10-1 (Microbial, Algal, and Fungal Biochemistry)
IT **443782-82-9P**, Botryolin A **443782-83-0P**, Botryolin B
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(triterpenoid polyethers botryolin A and botryolin B from green microalga Botryococcus)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:412607 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 135:166755
TITLE: Triple ring closing metathesis reaction: synthesis of adjacent cyclic ethers
AUTHOR(S): Heck, Marie-Pierre; Baylon, Christophe; Nolan, Steven P.; Mioskowski, Charles
CORPORATE SOURCE: Service des Molecules Marquees Departement de Biologie Cellulaire et Moleculaire, CEA-CE Saclay, Gif sur Yvette, F-91191, Fr.
SOURCE: Organic Letters (2001), 3(13), 1989-1991
CODEN: ORLEF7; ISSN: 1523-7060

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:166755
GI



I



II

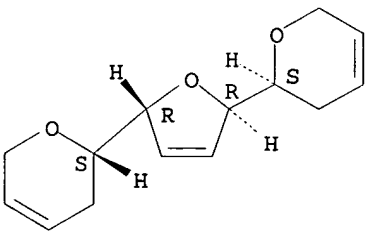
AB Adjacent tris(cyclic ethers) and enol ethers, e.g., I, have been synthesized in good yields for the first time via a triple olefin metathesis reaction using Grubbs' catalyst RuCl2(:C(H)Ph)(PCy3)2 (Cy = cyclohexyl), and the 1,3-dimesitylimidazol-2-ylidene ruthenium benzylidene catalyst RuCl2(:C(H)Ph)(PCy3)(IMes) ((IMes) = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene). Thus, allylic ether II when treated with Grubbs' catalyst gave I in 65% yield. The mesityl catalyst proved to be the most efficient catalyst in these transformations.

IT **353491-07-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and ruthenium-catalyzed ring closing metathesis of allylic ethers to cyclic ethers)

RN 353491-07-3 HCAPLUS

CN 2H-Pyran, 2,2'-[(2R,5R)-2,5-dihydro-2,5-furandiyl]bis[3,6-dihydro-, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 27-13 (Heterocyclic Compounds (One Hetero Atom))

IT 353491-05-1P **353491-07-3P** 353491-08-4P 353491-09-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and ruthenium-catalyzed ring closing metathesis of allylic ethers to cyclic ethers)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE

FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

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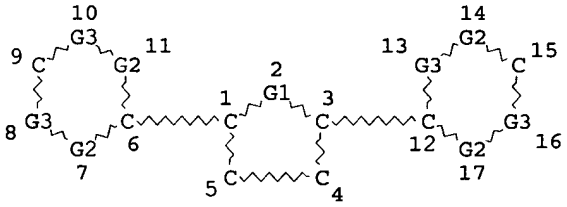


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VAR G2=C/N/O/S
VAR G3=C/N
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE
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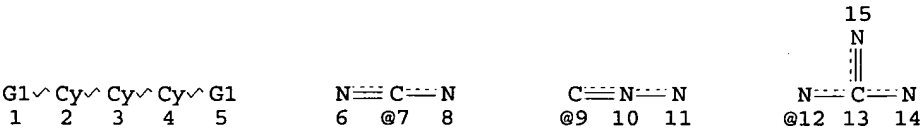


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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NUMBER OF NODES IS 15

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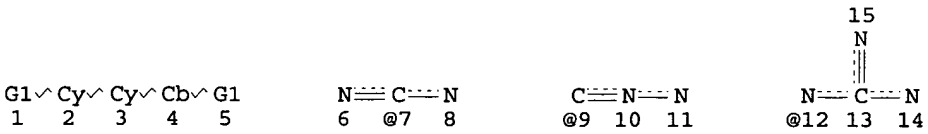

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ECOUNT IS E4 C E1 O AT 3
ECOUNT IS E6 C AT 4

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
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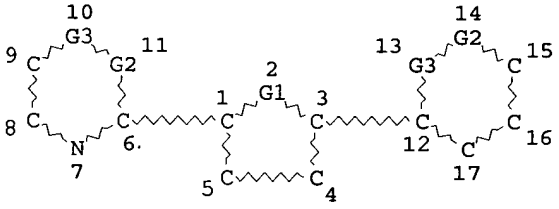
L16 127 SEA FILE=HCAPLUS ABB=ON PLU=ON L8
L17 30 SEA FILE=REGISTRY ABB=ON PLU=ON L2 AND L8
L19 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L17
L20 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND L19
L21 STR



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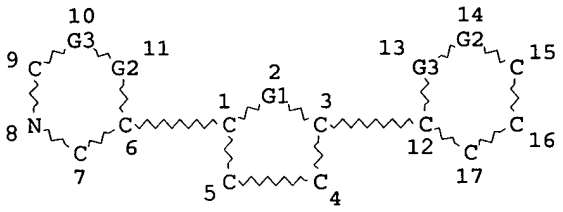
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L22 STR



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VAR G2=C/N/O/S
VAR G3=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
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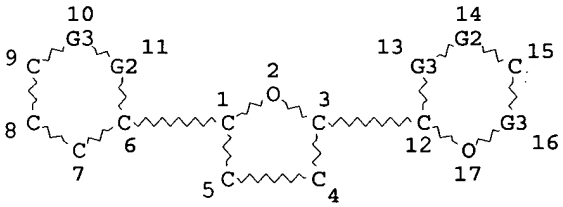

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L32 4 SEA FILE=REGISTRY SUB=L5 SSS FUL L28
L33 74 SEA FILE=REGISTRY ABB=ON PLU=ON L32 OR L27
L34 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L33
L35 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L34 OR L20
L36 159200 SEA FILE=HCAPLUS ABB=ON PLU=ON (PHARMA? OR DRUG? OR MEDICIN?)(2A)(CARRIER? OR DELIV?)
L37 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 AND L36
L38 470215 SEA FILE=HCAPLUS ABB=ON PLU=ON ?MICROB?
L39 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 AND L38
L40 43 SEA FILE=HCAPLUS ABB=ON PLU=ON L37 OR L39
L41 47 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 OR L35
L42 40 SEA FILE=HCAPLUS ABB=ON PLU=ON L41 NOT L35

=> d l42 1-42 ibib abs hitstr hitind

L42 ANSWER 1 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:13383 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 144:94404

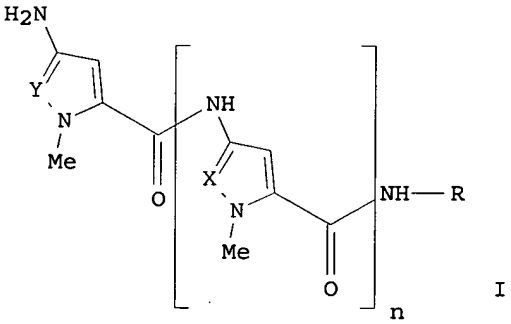
TITLE: Use of nitrogen heterocyclic compounds as **microbicides** for the treatment of sexually transmitted diseases
INVENTOR(S): Marcucci, Fabrizio
PATENT ASSIGNEE(S): Need Pharma S.R.L., Italy
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006000863	A1	20060105	WO 2005-IB1671	20050615

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: IT 2004-MI1248 A 20040622

GI



I

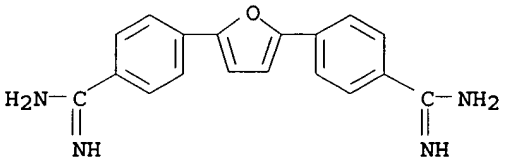
AB Object of the present invention is the use of nitrogen heterocyclic compds. and compns. comprising said compds. having the following general formula (I): wherein n is equal to zero or is an integer from 1 to 3; X and Y are equal to or different from each other and are chosen from -CH or N; R is a -Ph or naphthyl group substituted with one or more acid groups (optionally salified) of the type: SO3H, SO4H, SO3NH2, SO2H, PO4H2, PO3H2, PO3NH3, COOH and esters thereof as **microbicides.** Disclosed is also the pharmaceutical compns. comprising at least one nitrogen heterocyclic compound with **microbicidal** activity and compns. comprising said compds. and the use thereof in the prevention of sexually transmitted diseases. For example, disclosed compound with n as 1, X as -CH and R as naphthyl

disulfonate was found to have anti-HIV activity, which is not interfered with distamycin A.

IT **73819-26-8**, Furamidine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of nitrogen heterocyclic compds. as **microbicides** for treatment of sexually transmitted diseases)

RN 73819-26-8 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



IC ICM A61K031-4025
ICS A61K031-4155; A61K031-00; A61K031-40; A61P031-02; A61P031-04; A61P031-12; A61P031-18; A61P031-22; A61P033-02; A61P001-16

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST nitrogen heterocyclic compd **microbicide** sexually transmitted disease; antiHIV nitrogen naphthyl disulfonate distamycin A

IT **Drug delivery** systems
(capsules; use of nitrogen heterocyclic compds. as **microbicides** for treatment of sexually transmitted diseases)

IT **Drug delivery** systems
(gels; use of nitrogen heterocyclic compds. as **microbicides** for treatment of sexually transmitted diseases)

IT **Drug delivery** systems
(ointments, creams; use of nitrogen heterocyclic compds. as **microbicides** for treatment of sexually transmitted diseases)

IT **Drug delivery** systems
(tablets; use of nitrogen heterocyclic compds. as **microbicides** for treatment of sexually transmitted diseases)

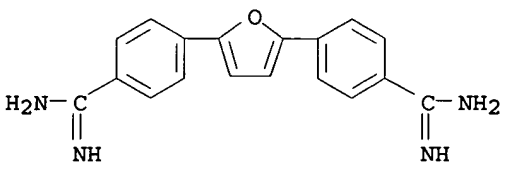
IT Anti-AIDS agents
Antimicrobial agents
Candida albicans
Chlamydia trachomatis
Combination chemotherapy
Hepatitis B virus
Hepatitis C virus
Human
Human herpesvirus
Human immunodeficiency virus 1
Human immunodeficiency virus 2
Neisseria gonorrhoeae
Papillomavirus
Sexually transmitted diseases
Treponema pallidum
Trichomonas vaginalis
(use of nitrogen heterocyclic compds. as **microbicides** for treatment of sexually transmitted diseases)

IT 155397-05-0 700344-74-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of nitrogen heterocyclic compds. as **microbicides** for treatment of sexually transmitted diseases)

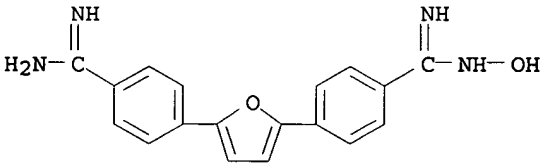
IT 100-33-4, Pentamidine 636-47-5, Distamycin A 1438-30-8, Congocidine 18378-89-7, Mitramycin 23491-45-4, Hoechst 33258 **73819-26-8**, Furamidine 98806-87-2 142482-63-1D, Bis-distamycin, analogs 848152-29-4, DB 2898
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of nitrogen heterocyclic compds. as **microbicides** for treatment of sexually transmitted diseases)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1283991 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 144:80510
TITLE: Unusual dehydroxylation of **antimicrobial** amidoxime prodrugs by cytochrome b5 and NADH cytochrome b5 reductase
AUTHOR(S): Saulter, Janelle Y.; Kurian, Joseph R.; Trepanier, Lauren A.; Tidwell, Richard R.; Bridges, Arlene S.; Boykin, David W.; Stephens, Chad E.; Anbazhagan, Mariappan; Hall, James Edwin
CORPORATE SOURCE: School of Pharmacy, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
SOURCE: Drug Metabolism and Disposition (2005), 33(12), 1886-1893
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Furamidine is an effective **antimicrobial** agent; however, oral potency of furamidine is poor. A prodrug of furamidine, 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime (DB289), has greatly improved oral potency. DB289 is transformed to furamidine via O-demethylation, and N-dehydroxylation reactions with four intermediate metabolites formed. The O-demethylation reactions have been shown to be catalyzed by cytochrome P 450. The enzymes catalyzing the reductive N-dehydroxylation reactions have not been determined The objective of this study was to identify the enzymes that catalyze N-dehydroxylation of metabolites M1, a monoamidoxime, and M2, a diamidoxime, formed during generation of furamidine. M1 and M2 metabolism was investigated using human liver microsomes and human soluble cytochrome b5 and NAD cytochrome b5 reductase, expressed in Escherichia coli. Kinetics of M1 and M2 reduction by human liver microsomes exhibited high affinity and moderate capacity. Metabolism was significantly inhibited by antibodies to cytochrome b5 and b5 reductase and by chemical inhibitors of b5 reductase. The amidoximes were efficiently metabolized by liver mitochondria, which contain cytochrome b5/b5 reductase, but not by liver cytosol, which contains minimal amts. of these proteins. Expressed cytochrome b5/b5 reductase, in the absence of any other proteins, efficiently catalyzed reduction of both amidoximes. Km values were similar to those for microsomes, and Vmax values were 33- to 36-fold higher in the recombinant system compared with microsomes. Minimal activity was seen with cytochrome b5 or b5 reductase alone or with cytochrome P 450 reductase alone or with cytochrome b5. These results indicate that cytochrome b5 and b5 reductase play a direct role in metabolic activation of DB289 to furamidine.
IT **73819-26-8**, Furamidine **591736-09-3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(unusual dehydroxylation of **antimicrobial** amidoxime prodrugs by cytochrome b5 and NADH cytochrome b5 reductase)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX

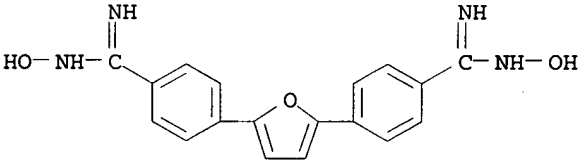
NAME)



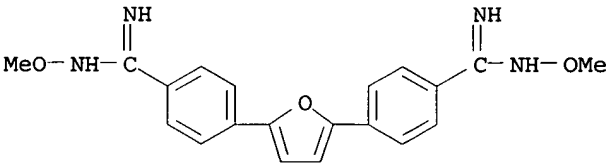
RN 591736-09-3 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-N-hydroxy- (9CI) (CA INDEX NAME)



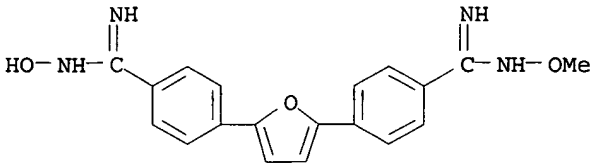
IT **186953-55-9 186953-56-0**, 2,5-Bis(4-amidinophenyl)furan-bis-O-methylamidoxime **475976-08-0**
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(unusual dehydroxylation of **antimicrobial** amidoxime prodrugs by cytochrome b5 and NADH cytochrome b5 reductase)
RN 186953-55-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)

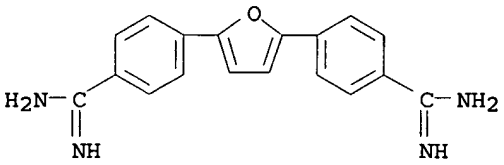


RN 475976-08-0 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



CC 1-2 (Pharmacology)
Section cross-reference(s): 63
IT **Drug delivery** systems
(prodrugs; unusual dehydroxylation of **antimicrobial** amidoxime prodrugs by cytochrome b5 and NADH cytochrome b5 reductase)
IT Enzyme kinetics
Human
Liver
Michaelis constant
Mitochondria
(unusual dehydroxylation of **antimicrobial** amidoxime prodrugs by cytochrome b5 and NADH cytochrome b5 reductase)
IT 9032-25-1, NADH cytochrome b5 reductase 9035-39-6, Cytochrome b5
73819-26-8, Furamidine **591736-09-3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(unusual dehydroxylation of **antimicrobial** amidoxime prodrugs by cytochrome b5 and NADH cytochrome b5 reductase)
IT **186953-55-9 186953-56-0**, 2,5-Bis(4-amidinophenyl)furan-bis-O-methylamidoxime **475976-08-0**
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(unusual dehydroxylation of **antimicrobial** amidoxime prodrugs by cytochrome b5 and NADH cytochrome b5 reductase)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1265621 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 144:16423
TITLE: Permeability and metabolism of potential prodrugs for the **antimicrobial** agent 2,5 bis(4-amidinophenyl)furan
AUTHOR(S): Saulter, Janelle Yvette
CORPORATE SOURCE: Univ. of North Carolina, Chapel Hill, NC, USA
SOURCE: (2005) 213 pp. Avail.: UMI, Order No. DA3170543
From: Diss. Abstr. Int., B 2005, 66(3), 1484
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **73819-26-8**, 2,5 Bis(4-amidinophenyl)furan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(permeability and metabolism of potential prodrugs for the **antimicrobial** agent 2,5 bis(4-amidinophenyl)furan)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



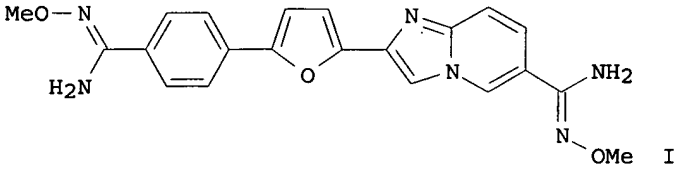
CC 1-2 (Pharmacology)
Section cross-reference(s): 63
ST prodrug metab **antimicrobial** amidinophenyl furan
IT **Antimicrobial** agents
Drug metabolism
(permeability and metabolism of potential prodrugs for the **antimicrobial** agent 2,5 bis(4-amidinophenyl)furan)
IT **Drug delivery** systems
(prodrugs; permeability and metabolism of potential prodrugs for the **antimicrobial** agent 2,5 bis(4-amidinophenyl)furan)
IT **73819-26-8**, 2,5 Bis(4-amidinophenyl)furan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(permeability and metabolism of potential prodrugs for the **antimicrobial** agent 2,5 bis(4-amidinophenyl)furan)

L42 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1026866 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 143:326361
TITLE: Preparation of dicationic imidazo[1,2-a]pyridines and 5,6,7,8-tetrahydroimidazo[1,2a]pyridines as antiprotozoal agents
INVENTOR(S): Boykin, David W.; Tidwell, Richard R.; Wilson, W. David; Ishmail, Mohammed A.
PATENT ASSIGNEE(S): The University of North Carolina At Chapel Hill, USA; Georgia State University Research Foundation, Inc.
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005086808	A2	20050922	WO 2005-US7566	2005 0308
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005282853	A1	20051222	US 2005-74565	2005 0308

PRIORITY APPLN. INFO.: US 2004-551091P P 2004 0308

OTHER SOURCE(S): MARPAT 143:326361
GI

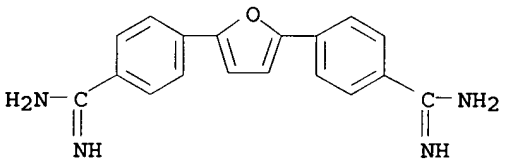


I

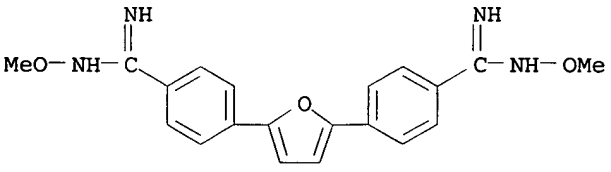
AB **Microbial** infection, including an infection from a protozoan pathogen, such as Trypanosoma brucei rhodesiense (T.b.r.) and Plasmodium falciparum (P.f.), in a subject in need thereof can be treated by administering to the subject an effective amount of a dicationic imidazopyridine compound or a dicationic tetrahydroimidazopyridine compound Processes for synthesizing dicationic imidazopyridines and dicationic tetrahydroimidazopyridines and the novel dicationic imidazopyridine and dicationic tetrahydroimidazopyridine compds. are given. I was prepared and was effective in tests on DNA affinities and in vitro testing against T.b.r. and P.f.

IT **73819-26-8**, Furamidine **186953-56-0**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation of dicationic imidazo[1,2-a]pyridines and 5,6,7,8-tetrahydroimidazo[1,2a]pyridines as antiprotozoal agents)

RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



IC ICM A61K
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 10

IT **73819-26-8**, Furamidine **186953-56-0**
RL: PAC (Pharmacological activity); BIOL (Biological study)

(preparation of dicationic imidazo[1,2-a]pyridines and 5,6,7,8-tetrahydroimidazo[1,2a]pyridines as antiprotozoal agents)

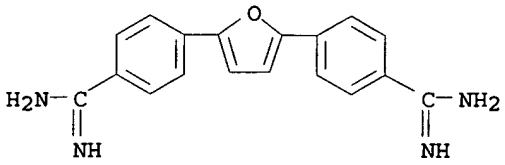
L42 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1026859 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 143:332486
TITLE: Dicationic compounds for activity against trichomonas vaginalis
INVENTOR(S): Boykin, David W.; Stephens, Chad E.; Secor, W. Evan; Crowell, Andrea L.; Kumar, Arvind
PATENT ASSIGNEE(S): Georgia State University Research Foundation, Inc., USA; The Government of the United States of America As
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005086754	A2	20050922	WO 2005-US7316	2005 0307

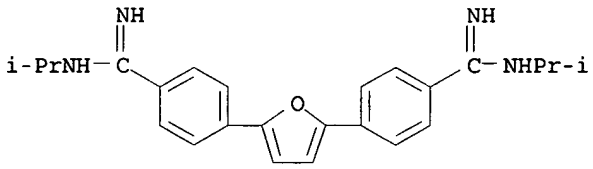
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-551089P P 2004 0308

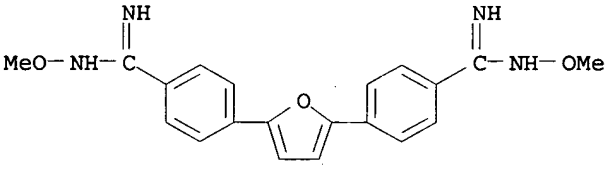
OTHER SOURCE(S): MARPAT 143:332486
AB Dicationic compds. for the treatment of T. vaginalis infections are described. The presently described compds. exhibit in vitro activity against metronidazole-sensitive and -resistant T. vaginalis isolates. Furthermore, the presently described compds. demonstrate IC50 concns. that were not elevated in the metronidazole resistant isolate, suggesting that their activity is not affected by parasite mechanisms that confer resistance to 5-nitroimidizoles.
IT **73819-26-8**, 2,5-Bis(4-amidinophenyl)furan
173420-56-9 186953-56-0 192525-52-3
442842-45-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dicationic compds. for activity against trichomonas vaginalis)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



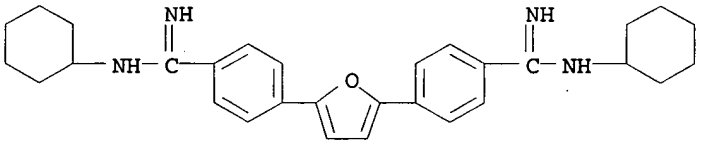
RN 173420-56-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



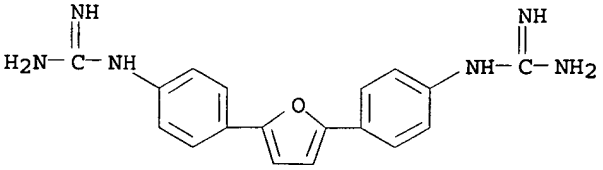
RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



RN 192525-52-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-cyclohexyl- (9CI) (CA INDEX NAME)



RN 442842-45-7 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis- (9CI) (CA INDEX NAME)



IC ICM A61K
CC 63-5 (Pharmaceuticals)

IT **Drug delivery** systems
(liposomes; dicationic compds. for activity against trichomonas vaginalis)
IT **Drug delivery** systems
(oral; dicationic compds. for activity against trichomonas vaginalis)
IT **Drug delivery** systems
(prodrugs; dicationic compds. for activity against trichomonas vaginalis)
IT 66-98-8, 4,4'-Diformyl-1,1'-biphenyl 106-51-4, 1,4-Benzoquinone, biological studies 68827-43-0, 4-Amidino-1,2-phenylenediamine **73819-26-8**, 2,5-Bis(4-amidinophenyl)furan 148344-30-3 **173420-56-9 186953-56-0 192525-52-3** 212829-51-1, 2,5-Benzofurandicarboxaldehyde 242807-42-7 **442842-45-7** 500714-77-2 790241-43-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dicationic compds. for activity against trichomonas vaginalis)

L42 ANSWER 6 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:324127 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 142:373841
TITLE: Preparation of novel amidines for treating **microbial** infections like human African trypanosomiasis and falciparum malaria
INVENTOR(S): Tidwell, Richard R.; Boykin, David; Brun, Reto; Stephens, Chad E.; Kumar, Arvind
PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA; Georgia State University Research Foundation, Inc.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005033065	A1	20050414	WO 2003-US27963	2003 0905

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2003-US27963 2003 0905

OTHER SOURCE(S): MARPAT 142:373841
GI

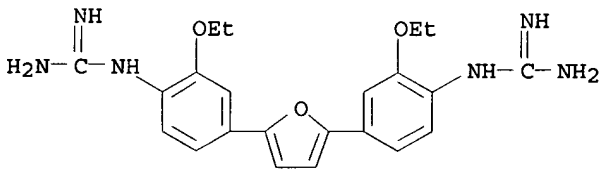
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Novel amidine and diamidine compds. (1st of 7 claimed Markush formulas shown as I; variables defined below; e.g. 4,4'-bis(6-amidinobenzimidazol-2-yl)-1,2-diphenylethane tetrahydrochloride (II)) may be useful in the treatment of **microbial** infections, including mycobacterial, fungal and protozoal infections. Pharmaceutical formulations comprising these compds. can be used in methods of treating **microbial** infections. Neither pharmacol. activity nor therapeutic use is claimed, but the effectiveness of 11 examples of the claimed compds. against Trypanosoma rhodesiense and Plasmodium falciparum is tabulated. Although the methods of preparation are not claimed, 9 example prepns. of claimed compds. and intermediates are included. For example, II was prepared (64 %) from 4,4'-diformyl-1,2-diphenylethane, 4-amidino-1,2-phenylenediamine hydrochloride hemihydrate and 1,4-benzoquinone in EtOH. For I: X' and X'' = alkyl, alkylene, O, oxy, oxyalkyl, alkyloxy, alkyloxyalkyl, and -C(O)NH(CH2)q-; m, n, p, and q = 0-10; L = hydroxyalkyl, 1,2-oxazole, 1,3-oxazole, Ph, naphthyl, pyrimidine, alkyl-substituted pyrimidine and -CH(CO2R11)- (R11 = H or alkyl); R1-R10 = H, alkyl, hydroxy, oxyalkyl, alkyloxy, halo, aryl, and Y, wherein at least one of R1-R10 = Y, and Y = -C(:NR12)NR13R14, -CH:NNHC(:NR12)NR13R14, and -NHC(NR12)NR13R14 (R12 = H, hydroxy, cycloalkyl, aryl, aralkyl, alkoxyl, hydroxycycloalkyl, alkoxycycloalkyl, hydroxyalkyl, aminoalkyl, acyloxy, and alkylaminoalkyl; R13 and R14 = H, hydroxy, alkyl, alkoxyalkyl, cycloalkyl, aryl, aralkyl, hydroxyalkyl, aminoalkyl, and alkylaminoalkyl; or R12 and R13 together = C2-C10 alkyl, hydroxyalkyl, or alkylene; or R12 and R13 together = (R15)j-substituted o-phenylene (j = 1-3, and R15 is H or Y)).

IT **423165-69-9P**, 2,5-Bis(3-ethoxy-4-guanidinophenyl)furan dihydrochloride **849623-37-6P**, 2,5-Bis(4-guanidino-3-methylthiophenyl)furan dihydrochloride **849623-42-3P**, 2,5-Bis[4-amidino-3-(methylthio)phenyl]furan
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of novel amidines for treating **microbial** infections like human African trypanosomiasis and falciparum malaria)

RN 423165-69-9 HCAPLUS

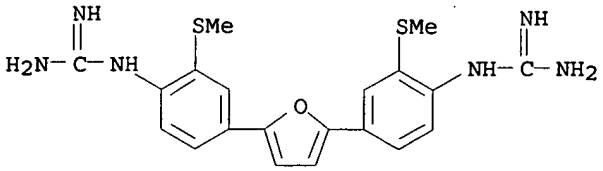
CN Guanidine, N,N'''-[2,5-furandiylbis(2-ethoxy-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

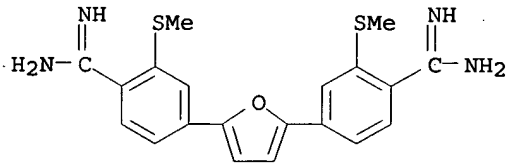
RN 849623-37-6 HCAPLUS

CN Guanidine, N,N'''-[2,5-furandiylbis[2-(methylthio)-4,1-phenylene]]bis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 849623-42-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[2-(methylthio)-(9CI) (CA INDEX NAME)



IC ICM C07C257-00
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 25, 27
IT Malaria
(falciparum; preparation of novel amidines for treating **microbial** infections like human African trypanosomiasis and falciparum malaria)
IT Antimalarials
Human
Plasmodium falciparum
Trypanosoma rhodesiense
Trypanosomicides
(preparation of novel amidines for treating **microbial** infections like human African trypanosomiasis and falciparum malaria)
IT Amidines
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel amidines for treating **microbial** infections like human African trypanosomiasis and falciparum malaria)
IT Infection
(trypanosomiasis; preparation of novel amidines for treating **microbial** infections like human African trypanosomiasis and falciparum malaria)
IT 423165-21-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of novel amidines for treating **microbial** infections like human African trypanosomiasis and falciparum malaria)
IT 26130-55-2P, 3-(Benzyloxy)benzenecarboximidamide 56806-77-0P, 1,4-Bis[4-[amino(imino)methyl]phenoxy]-2-butanol dihydrochloride 57928-60-6P, 4-(Benzyloxy)benzenecarboximidamide hydrochloride 77838-86-9P, 1,4-Bis(5-amidinobenzimidazol-2-yl)benzene 118499-88-0P, 1,2-Bis[4-[amino(imino)methyl]phenoxy]benzene

148344-27-8P, 1,4-Bis(5-amidinobenzimidazol-2-yl)-2,5-dimethylbenzene 204589-04-8P, 4,6-Bis(4-amidinophenyl)-2-methylpyrimidine 423165-59-7P, 2,5-Bis[2-hydroxy-4-[[(pyridin-2-yl)iminomethyl]amino]phenyl]furan dihydrochloride **423165-69-9P**, 2,5-Bis(3-ethoxy-4-guanidinophenyl)furan dihydrochloride 500713-52-0P, 9-[4-[Amino(imino)methyl]phenoxy]octyl phenyl ether hydrochloride 500713-59-7P, 4-[(3-Tolyl)methoxy]benzenecarboximidamide hydrochloride 500714-02-3P, 1,5-Bis[[3-[(imino)(isopropylamino)methyl]phenyl]methoxy]naphthalene 500714-04-5P, 1,5-Bis[[4-[(imino)(isopropylamino)methyl]phenyl]methoxy]naphthalene 500714-06-7P, 1,4-Bis[[4-[(imino)(isopropylamino)methyl]phenoxy]methyl]naphthalene 500714-08-9P, 1,5-Bis[3,6-bis(4,5-dihydro-1H-imidazol-2-yl)-9H-carbazol-9-yl]pentane 500714-29-4P, 5-[3-[Amino(imino)methyl]phenyl]-3-[4-[amino(imino)methyl]phenyl]isoxazole 500714-31-8P, 3-[3-[Amino(imino)methyl]phenyl]-5-[4-[amino(imino)methyl]phenyl]isoxazole 500714-34-1P, 1,4-Bis[(5-amidinoindol-2-yl)methyl]benzene 500714-40-9P, 1,2-Bis[4-[5-[(butylamino)(imino)methyl]benzimidazol-2-yl]phenyl]ethane 500714-42-1P, 2,7-Bis[[4-[(imino)(isopropylamino)methyl]phenyl]methoxy]naphthalene 500714-44-3P, 2,7-Bis[[3-[(imino)(isopropylamino)methyl]phenyl]methoxy]naphthalene 500714-46-5P, 1,4-Bis[6-(4,5-dihydro-1H-imidazol-2-yl)benzo[b]furan-2-yl]butane 500714-48-7P, 1,3-Bis[6-[(imino)(isopropylamino)methyl]benzo[b]furan-2-yl]propane 500714-53-4P, 1-[[5-[4-[[(sec-Butyl)amino](imino)methyl]phenoxy]pentyl]oxy]-3-[5-[(imino)(isopropylamino)methyl]benzimidazol-2-yl]benzene 500714-67-0P, 5-[4-[Amino(imino)methyl]phenyl]-2-[2-[4-[amino(imino)methyl]phenyl]ethyl]oxazole 500714-69-2P, 2,6-Bis(5-amidinobenzimidazol-2-yl)naphthalene 500714-75-0P, 1,2-Bis[4-(5-amidinobenzimidazol-2-yl)phenyl]ethane 500714-77-2P, 4,4'-Bis(5-amidinobenzimidazol-2-yl)-1,1'-biphenyl 500714-79-4P, Bis[4-(5-amidinobenzimidazol-2-yl)phenyl]methane 500714-81-8P, 1,2-Bis[4-(5-amidinobenzimidazol-2-yl)phenyl]cyclopropane 500714-83-0P, 2-(5-Amidinobenzimidazol-2-yl)-5-[2-[4-(5-amidinobenzimidazol-2-yl)phenyl]ethyl]thiophene 500714-92-1P, 2-[4-[2-(4-Methoxyphenyl)ethyl]phenyl]-1H-benzimidazole-5-carboximidamide 500714-93-2P, 2-[4-[2-(4-Ethylphenyl)ethyl]phenyl]-1H-benzimidazole-5-carboximidamide 500714-94-3P, 2-[4-[2-(4-Fluorophenyl)ethyl]phenyl]-1H-benzimidazole-5-carboximidamide 500714-95-4P, 2-[6-(4-Amidinophenyl)pyridin-2-yl]-1H-benzimidazole-5-carboximidamide 500714-97-6P, 2-(5-Amidinobenzoxazol-2-yl)-5-(4-amidinophenyl)furan 500714-98-7P, 2-(5-Amidinobenzimidazol-2-yl)-6-(4-amidinophenyl)phenol 500715-03-7P, 1,5-Bis[4-[[imino(phenyl)methyl]amino]phenoxy]pentane 500715-13-9P, 1,7-Bis[[4-[amino(imino)methyl]benzoyl]amino]heptane 634905-88-7P, 1,5-Bis[[3-[amino(imino)methyl]phenyl]methoxy]naphthalene 733735-45-0P, 1,3-Bis[[4-(4,5-dihydro-1H-imidazol-2-yl)phenoxy]methyl]benzene 763922-64-1P, 1,4-Bis[[4-(4,5-dihydro-1H-imidazol-2-yl)phenoxy]methyl]benzene 790241-42-8P, 4,4'-Bis(5-Amidinobenzimidazol-2-yl)biphenyl tetrahydrochloride 849623-20-7P, 2,6-Bis(4-amidinobenzimidazol-2-yl)naphthalene tetrahydrochloride 849623-21-8P, 4,4'-Bis(6-amidinobenzimidazol-2-yl)-1,2-diphenylethane tetrahydrochloride 849623-26-3P, 1-[4-(5-Amidinobenzimidazol-2-yl)phenyl]-2-[2-(5-amidinobenzimidazol-2-yl)thien-5-yl]ethane trihydrochloride 849623-33-2P, 2-(5-Amidinobenzimidazol-2-yl)-6-(4-amidinophenyl)pyridine triacetate **849623-37-6P**, 2,5-Bis(4-guanidino-3-methylthiophenyl)furan dihydrochloride 849623-40-1P, 2-(5-Amidinobenzimidazol-2-yl)-5-(4-amidino-2-methylphenyl)furan trihydrochloride 849623-41-2P, Methyl 4-[4-[amino(imino)methyl]phenoxy]-2-[2-[4-[amino(imino)methyl]phenoxy]ethyl]butanoate **849623-42-3P**

, 2,5-Bis[4-amidino-3-(methylthio)phenyl]furan
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of novel amidines for treating **microbial** infections like human African trypanosomiasis and falciparum malaria)

IT 98-01-1, 2-Furfuraldehyde, reactions 610-38-8, 3,4-Dinitrobromobenzene 1220-08-2, 4,4'-Diformyl-1,2-diphenylethane 1591-30-6, 4,4'-Dicyanobiphenyl 4701-17-1, 5-Bromothiophene-2-aldehyde 6345-68-2, 3-Benzyloxy-4-bromonitrobenzene 16532-79-9, 4-Bromophenylacetonitrile 17626-40-3, 3,4-Diaminobenzonitrile 31656-49-2, 2,6-Dicyanonaphthalene 34160-40-2, 6-Bromopyridine-2-carboxaldehyde 66717-58-6, 4-Amidino-1,2-phenylenediamine hydrochloride 78881-21-7, 4-Amino-3-methylbenzonitrile 126747-14-6, 4-Cyanophenylboronic acid 193361-76-1, 2,5-Bis(tributylstannyl)furan 347191-10-0, S-(2-Naphthylmethyl) pyridine-2-carboximidothioate hydrobromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of novel amidines for treating **microbial** infections like human African trypanosomiasis and falciparum malaria)

IT 66-98-8P, 4,4'-Diformyl-1,1'-biphenyl 5060-65-1P, 2,6-Diformylnaphthalene 57279-70-6P, 2-Nitro-5-bromophenetole 96463-58-0P, 2-(4-Bromophenyl)-3-(5-bromothien-2-yl)acrylonitrile 423165-37-1P, 2,5-Bis(3-ethoxy-4-nitrophenyl)furan 423165-42-8P, 2,5-Bis(2-benzyloxy-4-nitrophenyl)furan 423165-50-8P, 2,5-Bis(4-amino-3-ethyloxyphenyl)furan 423165-51-9P, 2,5-Bis(4-amino-2-hydroxyphenyl)furan 834884-79-6P, 6-(4-Cyanophenyl)pyridine-2-carboxaldehyde 849623-22-9P, 2-(4-Bromophenyl)-3-(5-bromothien-2-yl)propionitrile 849623-23-0P, 2-(4-Bromophenyl)-3-(5-bromothien-2-yl)propionic acid 849623-24-1P, 1-(4-Cyanophenyl)-2-(5-cyanothien-2-yl)ethane 849623-25-2P, 1-(4-Formylphenyl)-2-(5-formylthien-2-yl)ethane 849623-30-9P, 2-(5-Cyanobenzimidazol-2-yl)-6-(4-cyanophenyl)pyridine 849623-31-0P, 2-(5-Hydroxyamidinobenzimidazol-2-yl)-6-(4-hydroxyamidinophenyl)pyridine 849623-32-1P, 2-(5-Acetoxyamidinobenzimidazol-2-yl)-6-(4-acetoxyamidinophenyl)pyridine 849623-34-3P, 5-Bromo-2-nitrothioanisole 849623-35-4P, 2,5-Bis(4-nitro-3-methylthiophenyl)furan 849623-36-5P, 2,5-Bis(4-amino-3-methylthiophenyl)furan 849623-38-7P, 2-(4-Cyano-2-methylphenyl)-5-formylfuran 849623-39-8P, 2-(5-Cyanobenzimidazol-2-yl)-5-(4-cyano-2-methylphenyl)furan
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel amidines for treating **microbial** infections like human African trypanosomiasis and falciparum malaria)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 7 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:259874 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 142:322768
TITLE: **Microbicide** composition comprising a minor groove binder optionally in combination with an anti-HIV compound for prevention of sexually transmitted diseases
INVENTOR(S): Marcucci, Fabrizio
PATENT ASSIGNEE(S): Need Pharmaceuticals S.R.L., Italy
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025565	A1	20050324	WO 2004-IB2923	20040908

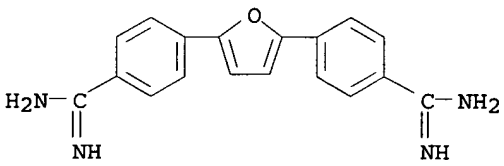
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2003-MI1754 A 20030912

AB A **microbicide** composition and the use thereof in the prophylaxis of the sexually transmitted diseases are described. The composition is characterized by containing (i) a DNA minor groove binder, e.g., Distamycin A, Mithramycin, Congocidine, Hoechst 33258, Pentamidine, Furamidine, etc., and (ii) an anti-HIV compound, e.g., surfactants such as N-onoxynol-9, sodium dodecylsulfate, C31G, and benzalkonium chloride, antibiotics such as magainin and protegrin, oxidizing agents such as chlorhexidine and hydrogen peroxide, anti-HIV and anti-CD4 antibodies, reverse transcriptase inhibitors, inhibitors of HIV attack and/or fusion to cells such as Suradista analogs, etc. For example, a tablet/capsule composition contained Distamycin A at the possible concns. ranging from 0.01 and 4%. The formulation contained cellulose (0 to 100%), hydroxypropyl Me cellulose (2 to 10%), Me cellulose (2 to 10%), crospovidone (2 to 5%), magnesium stearate (0.25 to 5%), corn starch (5 to 25%), lactic acid (0.05 to 6%), colloidal silicon dioxide (2 to 10%), and the combination of Distamycin A + Suradista. The ratio of Distamycin A and Suradista can be between 1:5 and 5%, preferably between 1:2 and 2:1, preferably about 1:1.

IT **73819-26-8**, Furamidine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)

RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



IC ICM A61K031-40
ICS A61P031-04; A61P031-18; A61P031-22

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkylbenzyldimethyl, chlorides; **microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)
IT Polyelectrolytes
(anionic; **microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)
IT Antibodies and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-HIV and anti-CD4; **microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)
IT **Drug delivery** systems
(capsules; **microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)
IT **Drug delivery** systems
(gels; **microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)
IT Anti-AIDS agents
Antibacterial agents
Antibiotics
Antimicrobial agents
Antiviral agents
Candida albicans
Chlamydia trachomatis
Combination chemotherapy
Contraceptives
Cytotoxicity
Drug toxicity
Fungicides
Hepatitis B virus
Hepatitis C virus
Human
Human herpesvirus 1
Human herpesvirus 2
Human immunodeficiency virus 1
Human immunodeficiency virus 2
Neisseria gonorrhoeae
Oxidizing agents
Papillomavirus
Protozoacides
Sexually transmitted diseases
Surfactants
Treponema pallidum
Trichomonas vaginalis
(**microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)
IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(minor groove, binders; **microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)
IT **Drug delivery** systems
(ointments, creams; **microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)
IT **Drug delivery** systems
(tablets; **microbicide** composition comprising minor groove

binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)

IT 9068-38-6, Reverse transcriptase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; **microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)

IT 55-56-1, Chlorhexidine 100-33-4, Pentamidine 151-21-3, Sodium dodecylsulfate, biological studies 636-47-5, Distamycin A 1438-30-8, Congocidine 7722-84-1, Hydrogen peroxide, biological studies 9000-07-1, Carrageenin 18378-89-7, Mithramycin 23491-45-4, Hoechst 33258 26027-38-3, N-Onoxynol-9 29321-75-3, PRO 2000 50851-57-5 **73819-26-8**, Furamidine 86903-77-7, C 31G 98806-87-2D, analogs 113041-69-3, Magainin 129618-40-2, Nevirapine 142482-63-1D, Bis-distamycin, analogs 147127-20-6, Tenofovir 163663-18-1, Protegrin 178870-32-1, UC 781 200139-38-4, Suradista 444944-54-1, Cyanovirin (synthetic) 848152-29-4, DB 2898
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (**microbicide** composition comprising minor groove binder optionally in combination with anti-HIV compound for prevention of sexually transmitted diseases)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE. FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:216611 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 142:291340
TITLE: Formulations, conjugates, and combinations of drugs for the treatment of neoplasms
INVENTOR(S): Nichols, James M.; Foley, Michael A.; Keith, Curtis; Padval, Mahesh; Elliott, Peter
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020913	A2	20050310	WO 2004-US27695	20040825
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005080075	A1	20050414	US 2004-925835	20040825

PRIORITY APPLN. INFO.: US 2003-497617P P 20030825

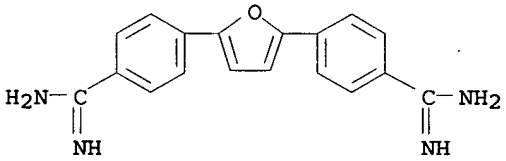
OTHER SOURCE(S): MARPAT 142:291340

AB The invention provides formulations and structural modifications for phenothiazine compds. which result in altered biodistribution, thereby reducing the occurrence of adverse reactions associated with this class of drug.

IT **73819-26-8**, 2,5-Bis(4-amidinophenyl)furan
73819-28-0 166601-09-8 166601-10-1
166601-11-2 173420-56-9 173420-67-2
179118-06-0 179118-08-2 179118-09-3
179118-17-3 179118-22-0 186953-55-9
186953-56-0, 2,5-Bis(4-amidinophenyl)furan-bis-O-methylamidoxime **186953-57-1 216308-16-6**
216308-17-7 216308-18-8 247032-11-7
247032-13-9 247032-15-1 247032-16-2
247032-17-3 247032-18-4 362059-27-6
648415-58-1 648415-59-2 648417-90-7
648417-91-8 847545-06-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulations and conjugates and combinations of drugs such as phenothiazines for treatment of neoplasms)

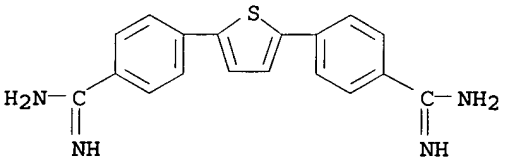
RN 73819-26-8 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



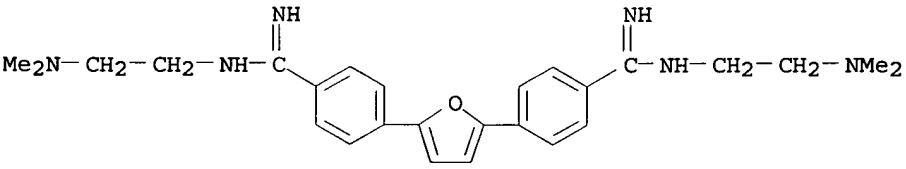
RN 73819-28-0 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-thiophenediyl)bis- (9CI) (CA INDEX NAME)



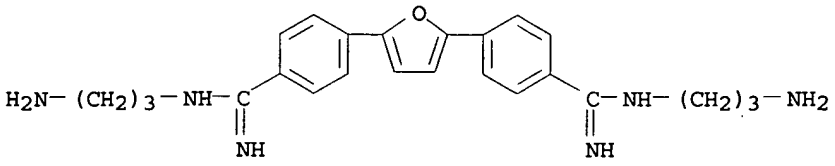
RN 166601-09-8 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)

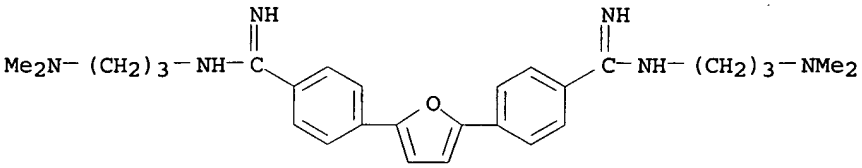


RN 166601-10-1 HCAPLUS

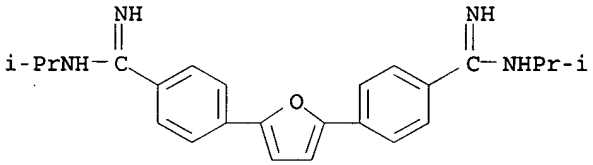
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(3-aminopropyl)- (9CI) (CA INDEX NAME)



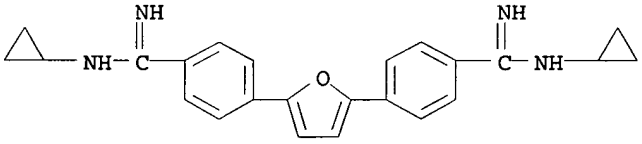
RN 166601-11-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



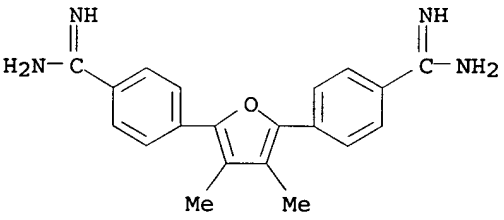
RN 173420-56-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)-(9CI) (CA INDEX NAME)



RN 173420-67-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-cyclopropyl-(9CI) (CA INDEX NAME)

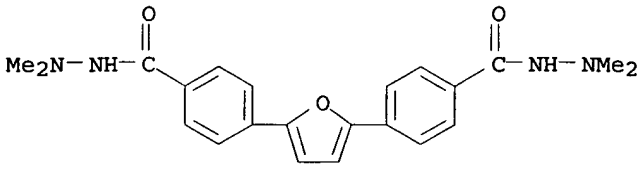


RN 179118-06-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3,4-dimethyl-2,5-furandiyl)bis-(9CI) (CA INDEX NAME)

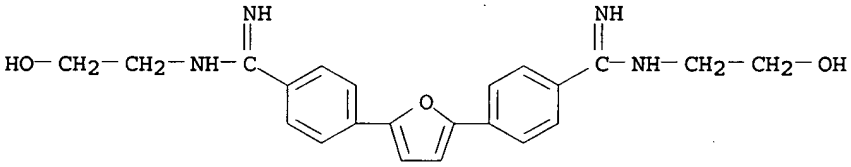


RN 179118-08-2 HCAPLUS
CN Benzoic acid, 4,4'-(2,5-furandiyl)bis-, bis(2,2-dimethylhydrazide)

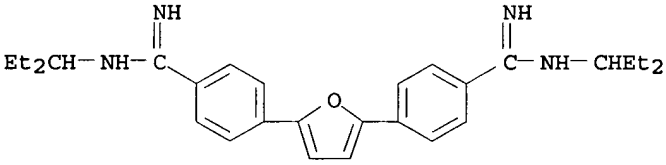
(9CI) (CA INDEX NAME)



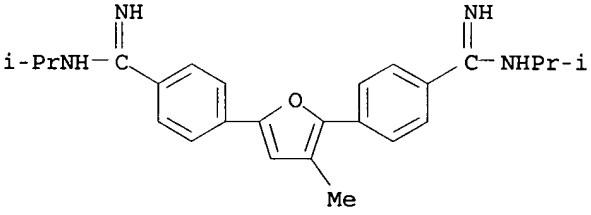
RN 179118-09-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



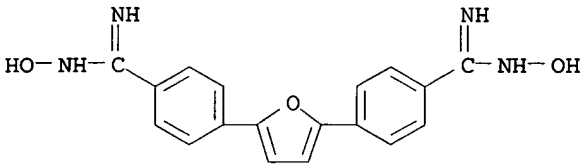
RN 179118-17-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-ethylpropyl)- (9CI) (CA INDEX NAME)



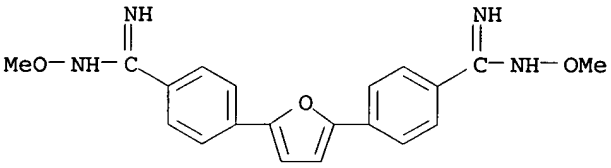
RN 179118-22-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3-methyl-2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



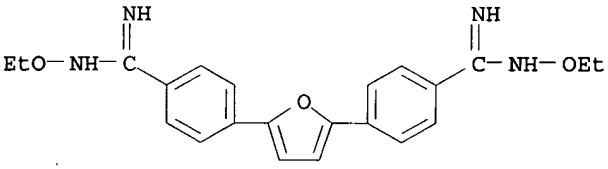
RN 186953-55-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



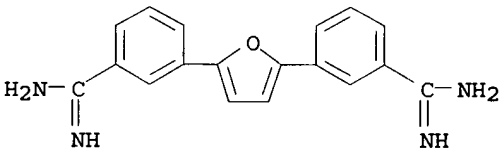
RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



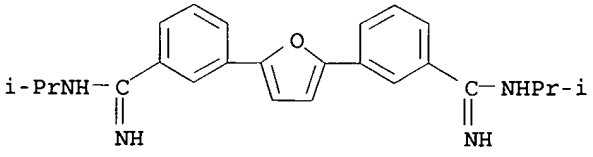
RN 186953-57-1 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-ethoxy- (9CI) (CA INDEX NAME)



RN 216308-16-6 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)

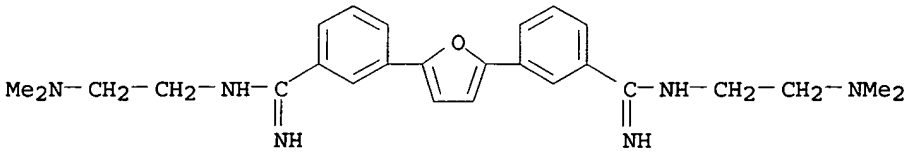


RN 216308-17-7 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)

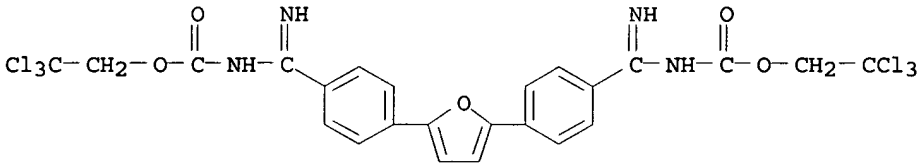


RN 216308-18-8 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis[N-[2-

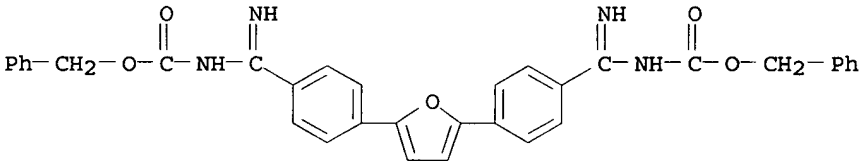
(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



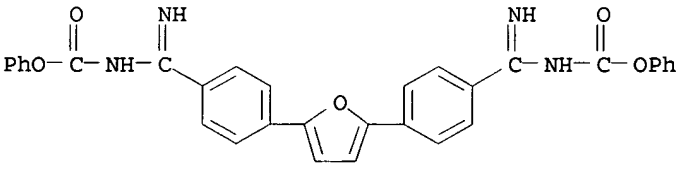
RN 247032-11-7 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)



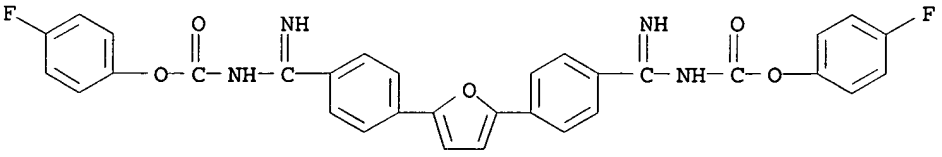
RN 247032-13-9 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



RN 247032-15-1 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, diphenyl ester (9CI) (CA INDEX NAME)

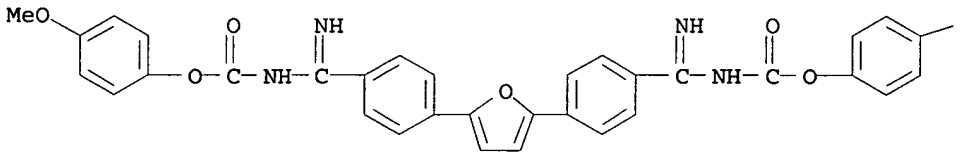


RN 247032-16-2 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-fluorophenyl) ester (9CI) (CA INDEX NAME)



RN 247032-17-3 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-methoxyphenyl) ester (9CI) (CA INDEX NAME)

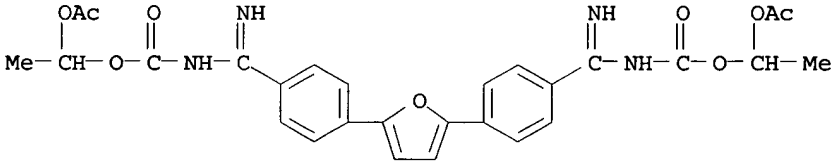
PAGE 1-A



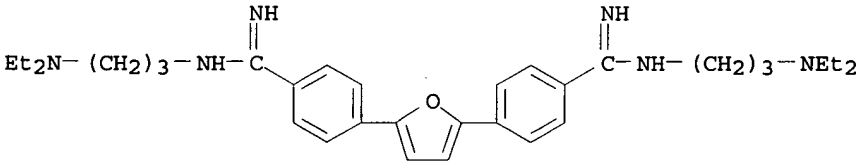
PAGE 1-B

OMe

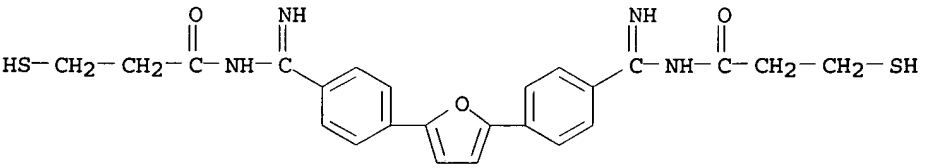
RN 247032-18-4 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis[1-(acetyloxy)ethyl] ester (9CI) (CA INDEX NAME)



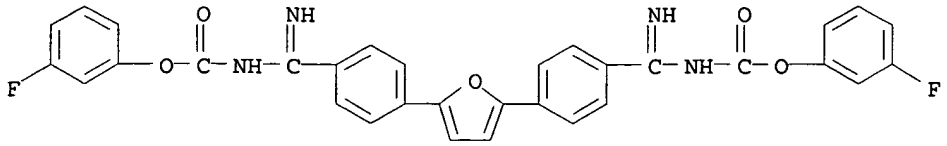
RN 362059-27-6 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[3-(diethylamino)propyl]- (9CI) (CA INDEX NAME)



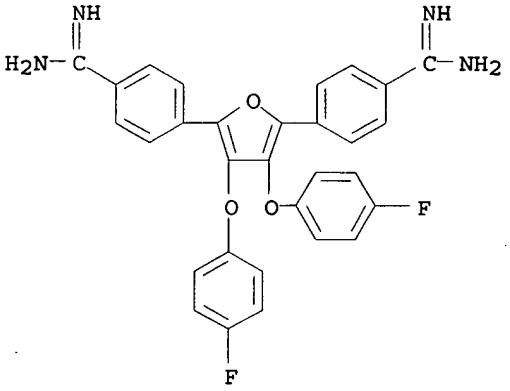
RN 648415-58-1 HCAPLUS
CN Propanamide, N,N'-[2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis[3-mercapto- (9CI) (CA INDEX NAME)



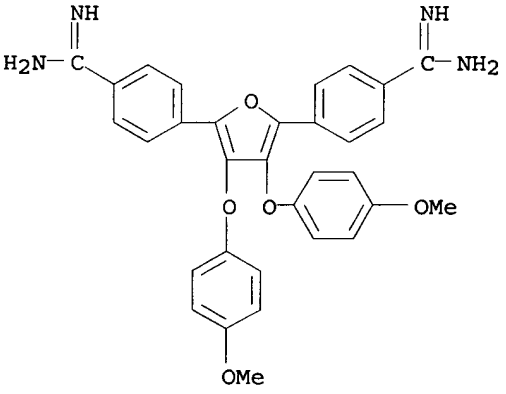
RN 648415-59-2 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(3-fluorophenyl) ester (9CI) (CA INDEX NAME)



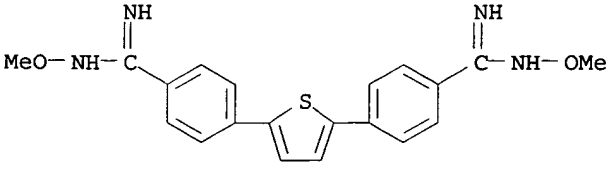
RN 648417-90-7 HCAPLUS
CN Benzenecarboximidamide, 4,4'-[3,4-bis(4-fluorophenoxy)-2,5-furandiyl]bis- (9CI) (CA INDEX NAME)



RN 648417-91-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-[3,4-bis(4-methoxyphenoxy)-2,5-furandiyl]bis- (9CI) (CA INDEX NAME)



RN 847545-06-6 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-thiophenediyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



IC ICM A61K
CC 1-6 (Pharmacology)
Section cross-reference(s): 63
IT **Drug delivery** systems
(liposomes; formulations and conjugates and combinations of drugs such as phenothiazines for treatment of neoplasms with decreased penetration of blood-brain barrier and CNS effects)
IT **Drug delivery** systems
(prodrugs; formulations and conjugates and combinations of drugs such as phenothiazines for treatment of neoplasms with decreased penetration of blood-brain barrier and CNS effects)
IT 50-53-3, Chlorpromazine, biological studies 101-62-2, Phenamidine 496-00-4, Dibromopropamidine 536-71-0, Diminazene 618-39-3, Benzamidine 653-03-2, Butaperazine 1225-64-5, Norchlorpromazine 1402-38-6, Actinomycin 1438-30-8, Netropsin 2095-24-1, Chlorfenethazine 3459-96-9, Amicarbalide 11056-06-7, Bleomycin 20830-81-3, Daunorubicin 33763-36-9, 3,7-Dicyanodibenzofuran 39389-47-4, Distamycin 41738-62-9, 3,7-Dicyanodibenzothiophene 41738-64-1, 3,7-Diaminodibenzothiophene 66639-24-5 67019-91-4, 3,7-Dibromodibenzofuran **73819-26-8**, 2,5-Bis(4-amidinophenyl)furan **73819-28-0** 74733-75-8, Bis(5-amidino-2-benzimidazolyl)methane 75846-15-0 75846-16-1 77838-87-0 80498-71-1 80498-77-7 83834-10-0, 3,7-Dibromodibenzothiophene 91371-12-9, 4,4'-Dibromo-2,2'-dinitrobiphenyl 101689-95-6 124076-65-9 148344-21-2 157168-41-7, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-2-ethylbutane 157168-42-8, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-2,3-diethyl-2-butene 157168-43-9, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-1-butene 157168-44-0, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-2-butene 157168-45-1, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-1-methylbutane 157168-46-2, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-1-methyl-1-butene 157168-47-3 157168-48-4, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-2-methyl-1,3-butadiene 157168-49-5, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]butane 157168-50-8, Bis[5-(2-imidazolyl)-2-benzimidazolyl]methane 157168-51-9, 1,3-Bis[5-(2-imidazolyl)-2-benzimidazolyl]propane 160522-87-2 160522-88-3 160522-89-4 165596-46-3 166601-05-4 **166601-09-8 166601-10-1 166601-11-2** **173420-56-9** 173420-58-1 173420-61-6 173420-63-8 **173420-67-2** 179118-03-7 179118-04-8 179118-05-9 **179118-06-0 179118-08-2 179118-09-3** 179118-10-6 **179118-17-3 179118-22-0** 186395-09-5 186395-18-6 186395-20-0 186395-22-2 186395-24-4 186395-25-5 186395-26-6 186395-28-8 186395-29-9 186395-30-2 **186953-55-9** **186953-56-0**, 2,5-Bis(4-amidinophenyl)furan-bis-O-methylamidoxime **186953-57-1** 190958-06-6 190958-12-4 190958-16-8 206532-38-9 212829-50-0 213972-16-8 216308-12-2 216308-13-3 216308-14-4 **216308-16-6** **216308-17-7 216308-18-8** 216502-98-6 216502-99-7 216503-00-3 216503-01-4 216503-02-5 216503-05-8 216503-06-9 216503-07-0 216503-08-1 216503-09-2 232940-82-8, 2,8-Dicyanodibenzofuran 232940-83-9 232940-84-0 242807-42-7 **247032-11-7** **247032-13-9 247032-15-1 247032-16-2** **247032-17-3 247032-18-4** 338945-24-7, 2,8-Dibenzofurandicarboximidamide **362059-27-6** 415718-06-8 415718-14-8 415718-17-1 415718-20-6 415718-26-2 415718-29-5 415718-32-0, 2,8-Dibenzothiophenedicarboximidamide 415718-35-3 415718-41-1, 3,7-Dibenzothiophenedicarboximidamide 415718-44-4 415718-47-7 415718-50-2 648415-33-2 648415-36-5 648415-42-3 648415-43-4 648415-44-5 648415-45-6 648415-46-7

648415-47-8 648415-48-9 648415-49-0 648415-50-3
648415-51-4 648415-52-5 648415-53-6 **648415-58-1**
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847545-05-5 **847545-06-6** 847545-07-7 847545-11-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulations and conjugates and combinations of drugs such as phenothiazines for treatment of neoplasms)

L42 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:120654 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 142:191226
TITLE: Combination of pentamidine or analog and antiproliferative agent drugs for the treatment of neoplasms
INVENTOR(S): Nichols, James M.; Lee, Margaret S.; Keith, Curtis T.; Zhang, Yanzhen; Gaw, Debra A.
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

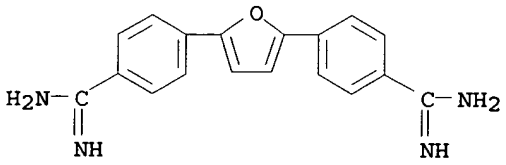
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005011572	A2	20050210	WO 2004-US23524	2004 0722
WO 2005011572	A3	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005054708	A1	20050310	US 2004-895561	2004 0721

PRIORITY APPLN. INFO.: US 2003-490759P P 2003 0728

OTHER SOURCE(S): MARPAT 142:191226
AB The invention features a method for treating a patient having a cancer or other neoplasm by administering to the patient pentamidine or a pentamidine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient. The combination of pentamidine and vinblastine provided improved antiproliferative activity against human non-small cell lung carcinoma A549 cells.
IT **73819-26-8**, 2,5-Bis(4-amidinophenyl)furan
73819-28-0 166601-10-1 166601-11-2
173420-56-9 179118-08-2 179118-22-0
186953-56-0, 2,5-Bis(4-amidinophenyl)furan-bis-O-methylamidoxime **216308-16-6 216308-18-8**
247032-11-7 247032-13-9 247032-15-1

247032-16-2 247032-17-3 247032-18-4
648415-32-1 648415-34-3 648415-37-6
648415-38-7 648415-39-8 648415-40-1
648415-41-2 648415-58-1 648415-59-2
648417-90-7 648417-91-8 648417-95-2
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of pentamidine or analog and antiproliferative agent drugs for treatment of neoplasms)

RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 73819-28-0 HCAPLUS
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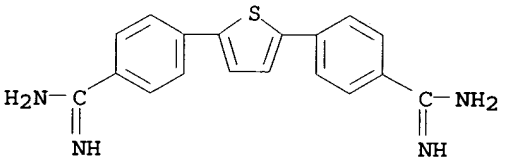

RN 166601-10-1 HCAPLUS
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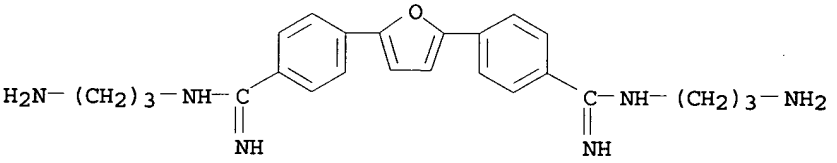
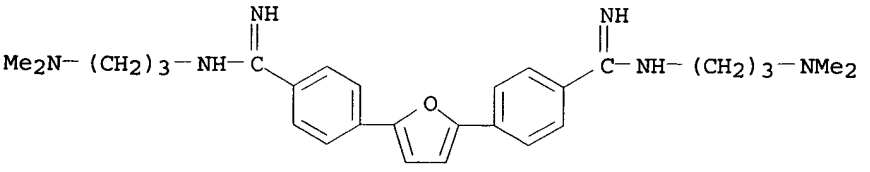
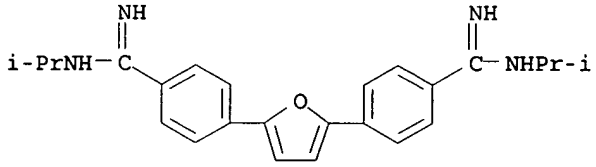


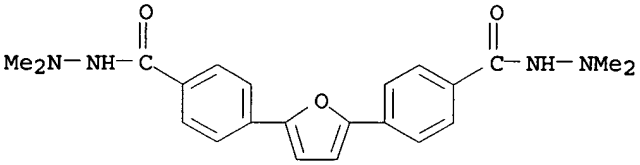
RN 166601-11-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



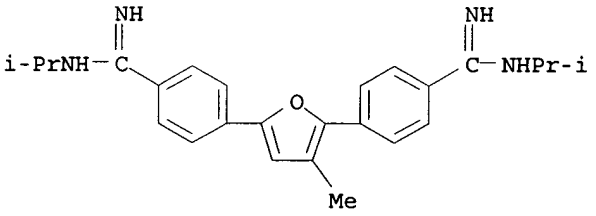
RN 173420-56-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 179118-08-2 HCAPLUS
CN Benzoic acid, 4,4'-(2,5-furandiyl)bis-, bis(2,2-dimethylhydrazide) (9CI) (CA INDEX NAME)



RN 179118-22-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3-methyl-2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 186953-56-0 HCAPLUS
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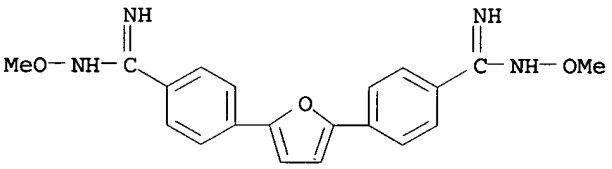
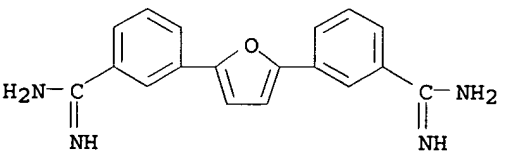
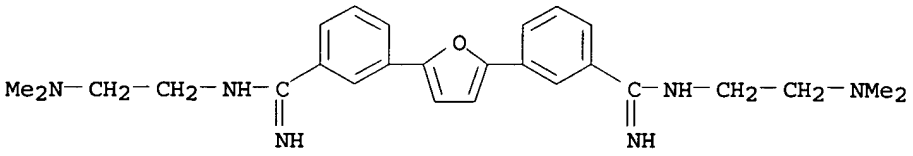


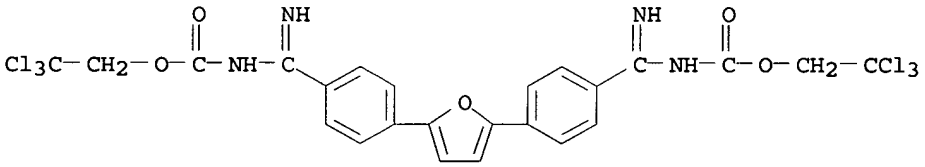
RN 216308-16-6 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



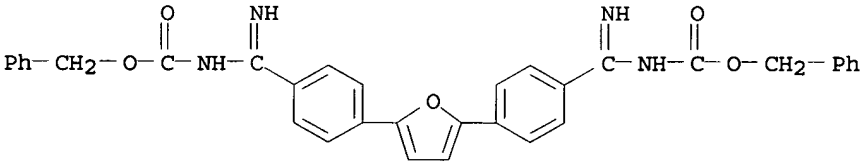
RN 216308-18-8 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis[N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



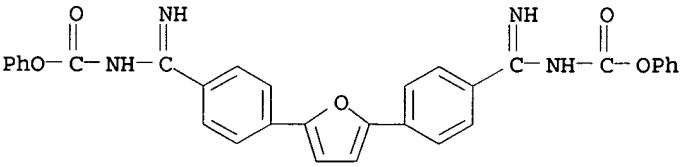
RN 247032-11-7 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)



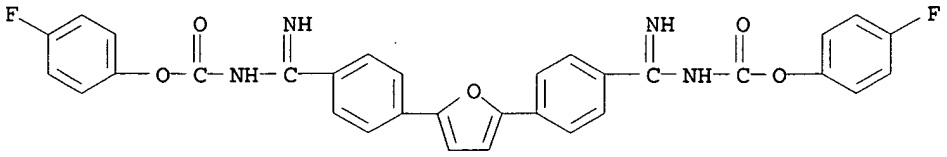
RN 247032-13-9 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



RN 247032-15-1 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, diphenyl ester (9CI) (CA INDEX NAME)

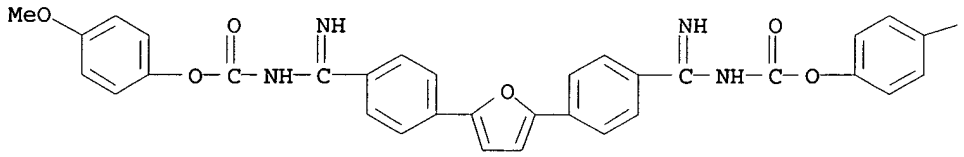


RN 247032-16-2 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-fluorophenyl) ester (9CI) (CA INDEX NAME)



RN 247032-17-3 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-methoxyphenyl) ester (9CI) (CA INDEX NAME)

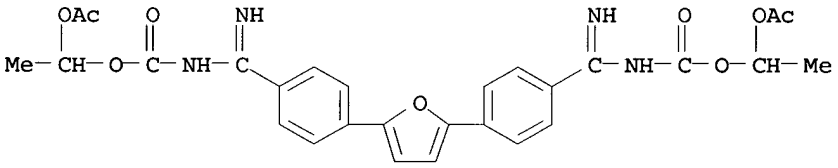
PAGE 1-A



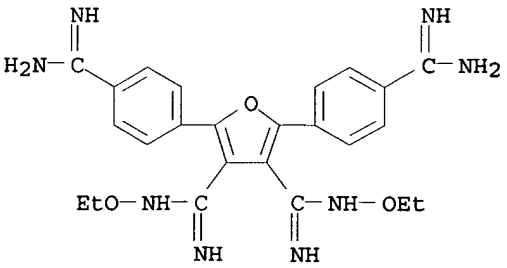
PAGE 1-B

OMe

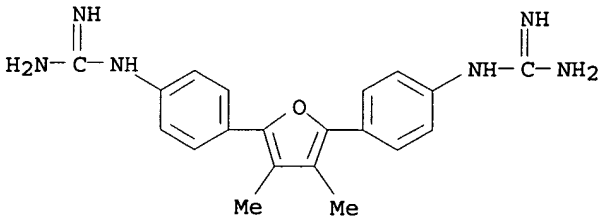
RN 247032-18-4 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis[1-(acetyloxy)ethyl] ester (9CI) (CA INDEX NAME)



RN 648415-32-1 HCAPLUS
CN 3,4-Furandicarboximidamide, 2,5-bis[4-(aminoiminomethyl)phenyl]-N,N''-diethoxy- (9CI) (CA INDEX NAME)



RN 648415-34-3 HCAPLUS
CN Guanidine, N,N'''-[(3,4-dimethyl-2,5-furandiyl)di-4,1-phenylene]bis- (9CI) (CA INDEX NAME)



RN 648415-37-6 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)

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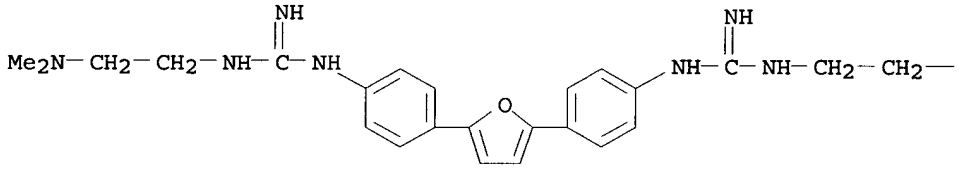

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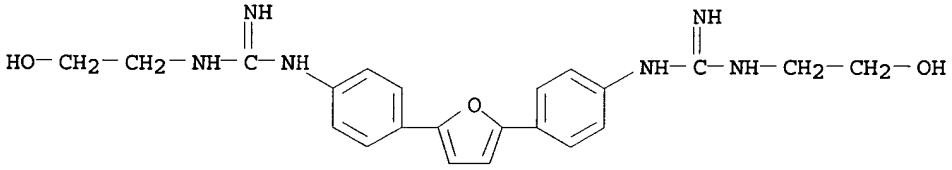
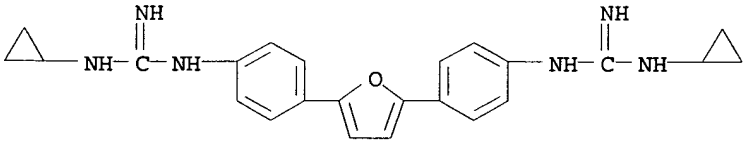
—NMe_2

RN 648415-38-7 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

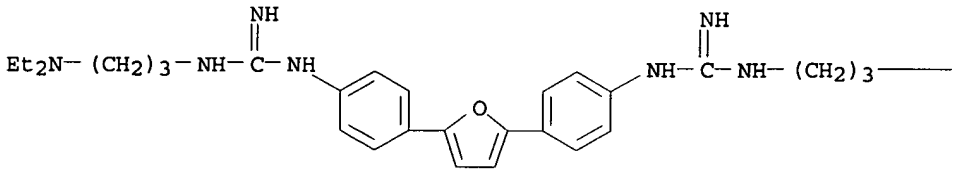


RN 648415-39-8 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-cyclopropyl- (9CI) (CA INDEX NAME)



RN 648415-40-1 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-[3-(diethylamino)propyl]- (9CI) (CA INDEX NAME)

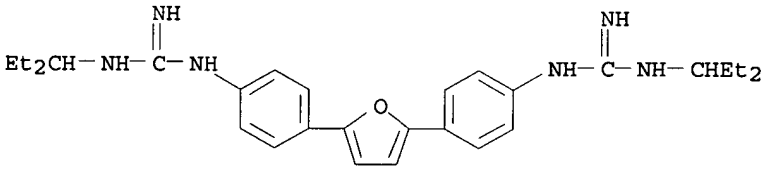
PAGE 1-A



PAGE 1-B

—NEt_2

RN 648415-41-2 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-(1-ethylpropyl)- (9CI) (CA INDEX NAME)



RN 648415-58-1 HCAPLUS
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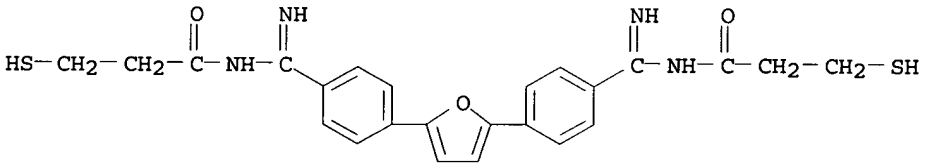
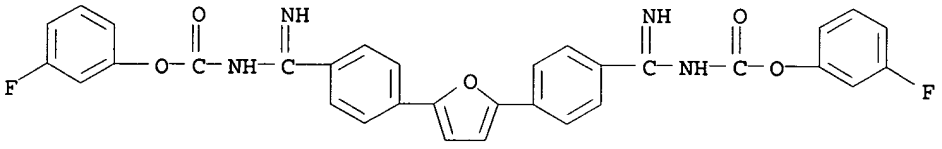


RN 648415-59-2 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(3-fluorophenyl) ester (9CI) (CA INDEX NAME)



RN 648417-90-7 HCAPLUS
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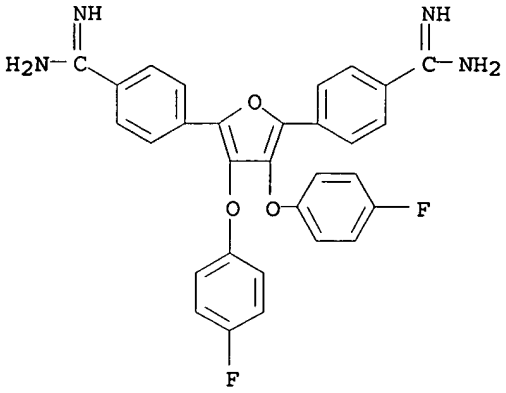

RN 648417-91-8 HCAPLUS
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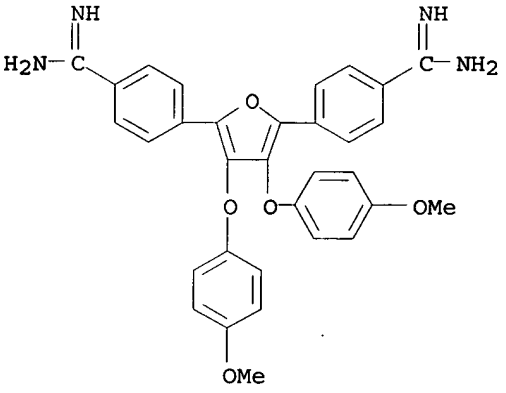
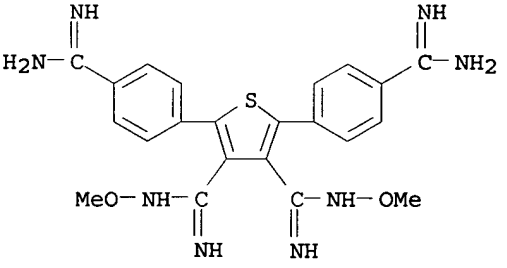


RN 648417-95-2 HCAPLUS
CN 3,4-Thiophenedicarboximidamide, 2,5-bis[4-(aminoiminomethyl)phenyl]-N,N''-dimethoxy- (9CI) (CA INDEX NAME)



IC ICM A61K
CC 1-6 (Pharmacology)
IT **Drug delivery** systems
(inhalants; combination of pentamidine or analog and antiproliferative agent drugs for treatment of neoplasms)
IT **Drug delivery** systems
(injections, i.m.; combination of pentamidine or analog and antiproliferative agent drugs for treatment of neoplasms)
IT **Drug delivery** systems

(injections, i.v.; combination of pentamidine or analog and antiproliferative agent drugs for treatment of neoplasms)

IT **Drug delivery** systems
(oral; combination of pentamidine or analog and antiproliferative agent drugs for treatment of neoplasms)

IT **Drug delivery** systems
(rectal; combination of pentamidine or analog and antiproliferative agent drugs for treatment of neoplasms)

IT 100-33-4, Pentamidine 100-33-4D, Pentamidine, analogs, derivs., salts 101-62-2, Phenamidine 104-32-5, Propamidine 122-06-5, Stilbamidine 495-99-8, Hydroxystilbamidine 496-00-4, Dibromopropamidine 536-71-0, Diminazene 618-39-3, Benzamidine 1402-38-6, Actinomycin 1438-30-8, Netropsin 3459-96-9, Amicarbalide 11056-06-7, Bleomycin 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin 25316-40-9, Adriamycin 33763-36-9, 3,7-Dicyanodibenzofuran 39389-47-4, Distamycin 41738-62-9, 3,7-Dicyanodibenzothiophene 41738-64-1, 3,7-Diaminodibenzothiophene 66639-24-5 67019-91-4, 3,7-Dibromodibenzofuran **73819-26-8**, 2,5-Bis(4-amidinophenyl)furan **73819-28-0** 74733-75-8, Bis(5-amidino-2-benzimidazolyl)methane 75846-15-0 75846-16-1 80498-71-1 80498-74-4 83834-10-0, 3,7-Dibromodibenzothiophene 91371-12-9, 4,4'-Dibromo-2,2'-dinitrobiphenyl 94345-47-8, Heptamidine 100562-53-6 101689-95-6 124076-61-5, Butamidine 124076-65-9 148344-21-2 157168-41-7, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-2-ethylbutane 157168-42-8, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-2,3-diethyl-2-butene 157168-43-9, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-1-butene 157168-44-0, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-2-butene 157168-45-1, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-1-methylbutane 157168-46-2, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]-1-methyl-1-butene 157168-48-4 157168-49-5, 1,4-Bis[5-(2-imidazolyl)-2-benzimidazolyl]butane 157168-50-8, Bis[5-(2-imidazolyl)-2-benzimidazolyl]methane 157168-51-9, 1,3-Bis[5-(2-imidazolyl)-2-benzimidazolyl]propane 160522-89-4 161374-52-3, Nonamidine 165596-46-3 166601-05-4 **166601-10-1 166601-11-2** 168637-58-9 **173420-56-9** 173420-58-1 173420-61-6 173420-63-8 179118-03-7 179118-04-8 179118-05-9 **179118-08-2** 179118-10-6 **179118-22-0** 186395-09-5 186395-18-6 186395-20-0 186395-22-2 186395-24-4 186395-25-5 186395-26-6 186395-27-7 186395-28-8 186395-29-9 186395-30-2 **186953-56-0**, 2,5-Bis(4-amidinophenyl)furan-bis-O-methylamidoxime 190958-06-6 190958-12-4 190958-16-8 200878-34-8 212829-50-0 213972-16-8 216308-12-2 216308-13-3 216308-14-4 **216308-16-6** **216308-18-8** 216502-98-6 216502-99-7 216503-00-3 216503-01-4 216503-02-5 216503-05-8 216503-06-9 216503-07-0 216503-08-1 216503-09-2 219483-82-6 232940-82-8, 2,8-Dicyanodibenzofuran 232940-83-9 232940-84-0 242807-42-7 **247032-11-7 247032-13-9 247032-15-1 247032-16-2 247032-17-3 247032-18-4** 338945-24-7, 2,8-Dibenzofurandicarboximidamide 415718-14-8 415718-17-1 415718-20-6 415718-26-2 415718-29-5 415718-32-0, 2,8-Dibenzothiophenedicarboximidamide 415718-35-3 415718-41-1, 3,7-Dibenzothiophenedicarboximidamide 415718-44-4 415718-47-7 415718-50-2 **648415-32-1** 648415-33-2 **648415-34-3** 648415-36-5 **648415-37-6 648415-38-7 648415-39-8 648415-40-1 648415-41-2** 648415-42-3 648415-43-4 648415-44-5 648415-45-6 648415-46-7 648415-47-8 648415-48-9 648415-49-0 648415-50-3 648415-51-4 648415-52-5 648415-53-6 648415-54-7 648415-55-8 **648415-58-1 648415-59-2 648417-90-7 648417-91-8** 648417-92-9 648417-93-0 648417-94-1 **648417-95-2**

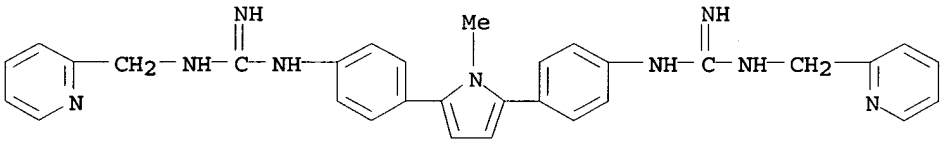
648417-96-3 648417-97-4 648418-01-3
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of pentamidine or analog and antiproliferative agent drugs for treatment of neoplasms)

L42 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:6494 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 143:193871
TITLE: Synthesis of dicationic 2,5-diarylpyrroles
AUTHOR(S): Arafa, Reem K.; Brun, Reto; Werbovetz, Karl A.; Tanious, Farial A.; Wilson, W. David; Boykin, David W.
CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Heterocyclic Communications (2004), 10(6), 423-428
CODEN: HCOMEX; ISSN: 0793-0283
PUBLISHER: Freund Publishing House Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:193871

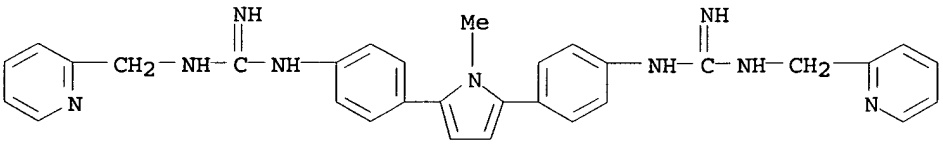
AB A new series of dicationic reversed amidine derivs. and a substituted guanidine analog of 2,5-diarylpyrrole obtained starting from the corresponding 2,5-bis(aminoaryl)pyrroles are reported. The results of DNA binding studies and **antimicrobial** screening assays for these compds. are presented.

IT **861806-23-7P 861806-34-0P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, DNA binding, and **antimicrobial** activity of dicationic diarylpyrroles)

RN 861806-23-7 HCAPLUS
CN Guanidine, N,N'''-[(1-methyl-1H-pyrrole-2,5-diyl)di-4,1-phenylene]bis[N'-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 861806-34-0 HCAPLUS
CN Guanidine, N,N'''-[(1-methyl-1H-pyrrole-2,5-diyl)di-4,1-phenylene]bis[N'-(2-pyridinylmethyl)-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

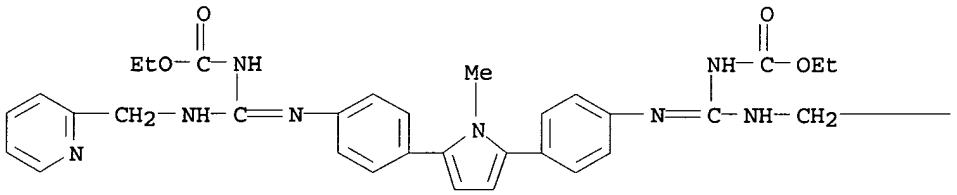
IT **861806-22-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, DNA binding, and **antimicrobial** activity of dicationic diarylpyrroles)

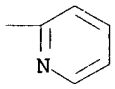
RN 861806-22-6 HCAPLUS

CN Carbamic acid, [(1-methyl-1H-pyrrole-2,5-diyl)bis[4,1-phenyleneimino[[(2-pyridinylmethyl)amino]methylidyne]]]bis-, diethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 6

ST dicationic diaryl pyrrole prepn DNA binding **antimicrobial** ; reversed dicationic amidine deriv prepn reaction; aminoaryl pyrrole prepn reaction

IT **Antimicrobial** agents
Leishmania donovani
Plasmodium falciparum
Trypanosoma rhodesiense
(synthesis, DNA binding, and **antimicrobial** activity of dicationic diarylpyrroles)

IT DNA
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(synthesis, DNA binding, and **antimicrobial** activity of dicationic diarylpyrroles)

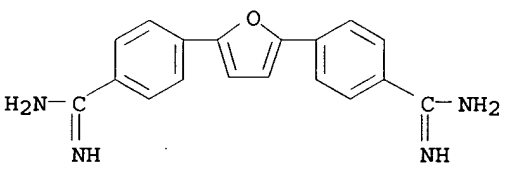
IT **861806-23-7P** 861806-28-2P 861806-29-3P 861806-30-6P
861806-31-7P 861806-32-8P 861806-33-9P **861806-34-0P**
861806-35-1P 861806-36-2P 861806-38-4P 861806-39-5P
861806-40-8P 861806-41-9P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, DNA binding, and **antimicrobial** activity of dicationic diarylpyrroles)

IT 99-81-0, 4-Nitrophenacyl bromide 100-19-6, p-Nitroacetophenone
121-89-1, m-Nitroacetophenone 3731-51-9, 2-(Aminomethyl)pyridine
16182-04-0 347191-10-0 347191-23-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis, DNA binding, and **antimicrobial** activity of dicationic diarylpyrroles)

IT 108791-66-8P 137596-49-7P 137596-50-0P 162878-72-0P
861806-21-5P **861806-22-6P** 861806-24-8P 861806-25-9P
861806-26-0P 861806-27-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP

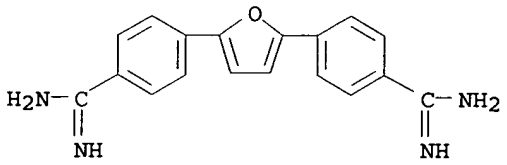
(Preparation); RACT (Reactant or reagent)
(synthesis, DNA binding, and **antimicrobial** activity of dicationic diarylpyrroles)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:848343 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 142:19722
TITLE: DB75, a novel trypanocidal agent, disrupts mitochondrial function in Saccharomyces cerevisiae
AUTHOR(S): Lanteri, Charlotte A.; Trumpower, Bernard L.; Tidwell, Richard R.; Meshnick, Steven R.
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, University of North Carolina, Chapel Hill, NC, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2004), 48(10), 3968-3974
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aromatic diamidines represent a class of compds. with broad-spectrum **antimicrobial** activity; however, their development is hindered by a lack of understanding of their mechanism of **antimicrobial** action. DB75 [2,5-bis(4-amidinophenyl)furan] is a trypanocidal aromatic diamidine that was originally developed as a structural analog of the antitrypanosomal agent pentamidine. DB289, a novel orally active prodrug of DB75, has undergone phase IIb clin. trials for early-stage human African trypanosomiasis, Pneumocystis jiroveci carinii pneumonia, and malaria. The purpose of this study was to investigate mechanisms of action of DB75 using Saccharomyces cerevisiae as a model organism. The results of this investigation suggest that DB75 inhibits mitochondrial function. Yeast cells relying upon mitochondrial metabolism for energy production are especially sensitive to DB75. DB75 localizes (by fluorescence) within the mitochondria of living yeast cells and collapses the mitochondrial membrane potential in isolated yeast mitochondria. Furthermore, addition of DB75 to yeast cells or isolated rat liver mitochondria results in immediate uncoupling of oxidative phosphorylation and subsequent inhibition of respiration. It is concluded that the mitochondrion is a cellular target of DB75 in yeast cells and anticipate that the results of this study will aid in the target-based design of new **antimicrobial** aromatic diamidines.
IT **73819-26-8**, 2,5-Bis(4-amidinophenyl)furan
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(DB75 as novel trypanocidal agent disrupts mitochondrial function in Saccharomyces cerevisiae)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



CC 10-2 (Microbial, Algal, and Fungal Biochemistry)
IT **73819-26-8**, 2,5-Bis(4-amidinophenyl)furan
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(DB75 as novel trypanocidal agent disrupts mitochondrial function in Saccharomyces cerevisiae)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

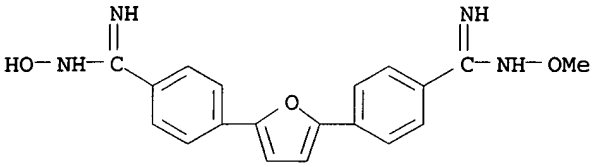
L42 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:566930 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 141:199478
TITLE: O-Alkoxyamidine Prodrugs of Furamidine: In Vitro Transport and Microsomal Metabolism as Indicators of in Vivo Efficacy in a Mouse Model of Trypanosoma brucei rhodesiense Infection
AUTHOR(S): Ansede, John H.; Anbazhagan, Mariappan; Brun, Reto; Easterbrook, Judy D.; Hall, James Edwin; Boykin, David W.
CORPORATE SOURCE: Division of Drug Delivery and Disposition School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599-7360, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(17), 4335-4338
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:199478
AB Five O-alkoxyamidine analogs of the prodrug 2,5-bis[4-methoxyamidinophenyl]furan were synthesized and evaluated against Trypanosoma brucei rhodesiense in the STIB900 mouse model by oral administration. The observed in vivo activity of these prodrugs demonstrates that compds. with an O-methoxyamidine or O-ethoxyamidine group effectively cured all trypanosome-infected mice, whereas prodrugs with larger side-chains did not completely cure the mice. Permeability across Caco-2 cell monolayers and microsomal metabolism were used to identify the underlying mechanisms of prodrug efficacy.
IT **73819-26-8**, Furamidine
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



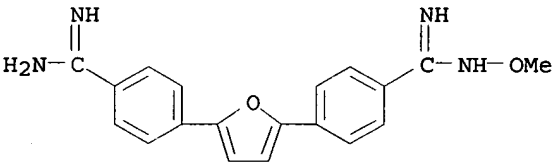
IT **475976-08-0 591735-77-2 591736-09-3 743438-64-4 743438-66-6 743438-67-7 743438-68-8**
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics);

BIOL (Biological study)
(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)

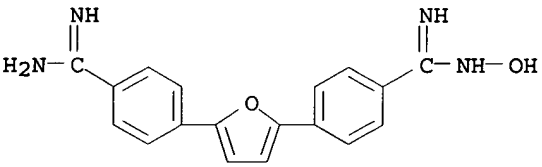
RN 475976-08-0 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



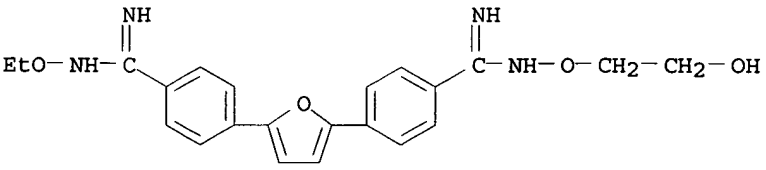
RN 591735-77-2 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



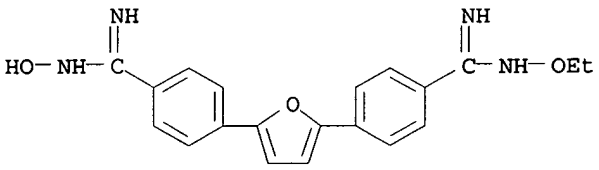
RN 591736-09-3 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-N-hydroxy- (9CI) (CA INDEX NAME)



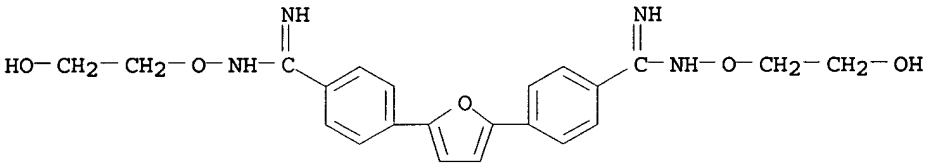
RN 743438-64-4 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-[(ethoxyamino)iminomethyl]phenyl]-2-furanyl]-N-(2-hydroxyethoxy)- (9CI) (CA INDEX NAME)



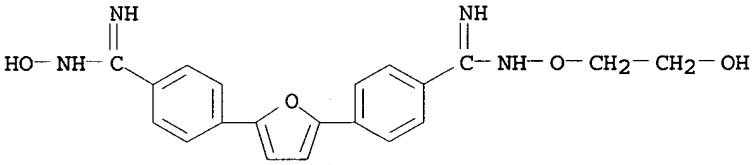
RN 743438-66-6 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-[(ethoxyamino)iminomethyl]phenyl]-2-furanyl]-N-hydroxy- (9CI) (CA INDEX NAME)



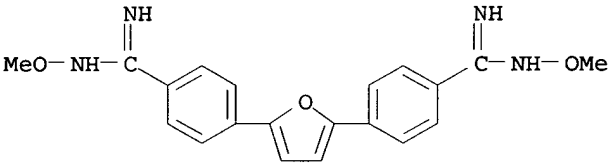
RN 743438-67-7 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(2-hydroxyethoxy)- (9CI) (CA INDEX NAME)



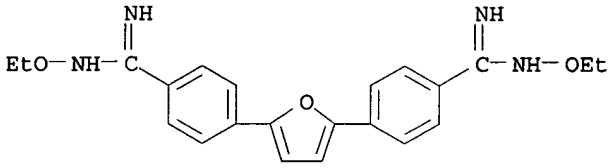
RN 743438-68-8 HCAPLUS
CN Benzenecarboximidamide, N-hydroxy-4-[5-[4-[[(2-hydroxyethoxy)amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



IT **186953-56-0P 186953-57-1P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)
RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)

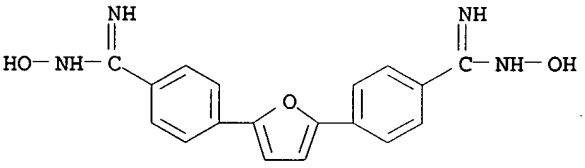


RN 186953-57-1 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-ethoxy- (9CI) (CA INDEX NAME)

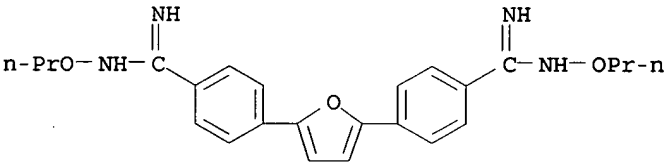


IT **186953-55-9P 582300-97-8P 743438-61-1P**
743438-62-2P 743438-63-3P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)

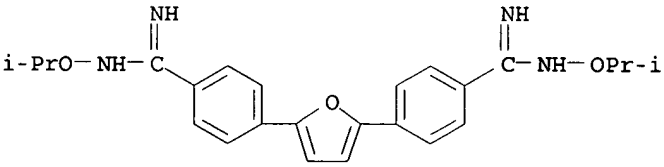
RN 186953-55-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



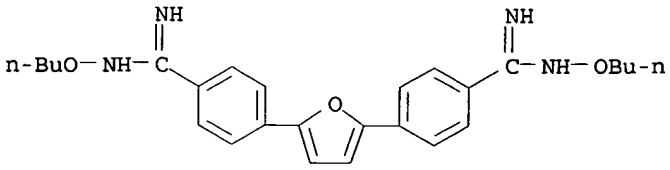
RN 582300-97-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-propoxy- (9CI) (CA INDEX NAME)



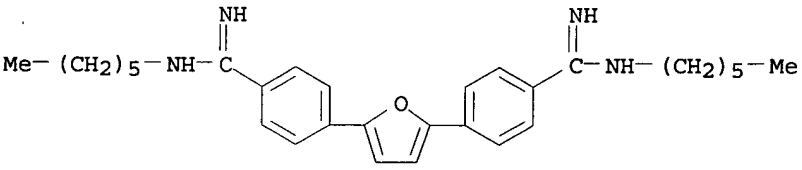
RN 743438-61-1 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethoxy)- (9CI) (CA INDEX NAME)



RN 743438-62-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-butoxy- (9CI) (CA INDEX NAME)



RN 743438-63-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hexyl- (9CI) (CA INDEX NAME)

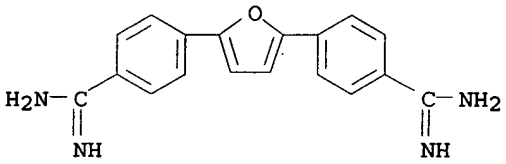


CC 1-3 (Pharmacology)
Section cross-reference(s): 63
IT **Drug delivery** systems
(prodrugs; in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)
IT **73819-26-8**, Furamidine
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)
IT **475976-08-0 591735-77-2 591736-09-3 743438-64-4 743438-66-6 743438-67-7 743438-68-8**
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)
IT **186953-56-0P 186953-57-1P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)
IT **186953-55-9P 582300-97-8P 743438-61-1P 743438-62-2P 743438-63-3P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in vitro transport and microsomal metabolism of O-alkoxyamidine prodrugs of furamidine as indicators of in vivo efficacy in mouse model of Trypanosoma brucei rhodesiense infection)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

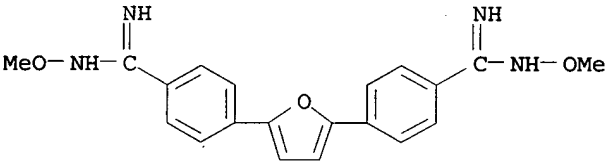
L42 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:539222 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 142:32481
TITLE: Distribution and quantitation of the anti-trypanosomal diamidine 2,5-bis(4-amidinophenyl)furan (DB75) and its N-methoxy prodrug DB289 in murine brain tissue
AUTHOR(S): Sturk, Lisa M.; Brock, Jacqueline L.; Bagnell, C. Robert; Hall, James E.; Tidwell, Richard R.
CORPORATE SOURCE: Department of Pathology and Lab. Medicine, Brinkhous-Bullitt Building, School of Medicine, Chapel Hill, NC, 27599, USA
SOURCE: Acta Tropica (2004), 91(2), 131-143
CODEN: ACTRAQ; ISSN: 0001-706X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The current epidemic of sleeping sickness, also known as human African trypanosomiasis in sub-Saharan Africa places nearly 60 million people at risk for developing this life threatening infection. Although effective treatments for early-stage sleeping sickness exist, these drugs usually require extended dosing schedules and i.v. administration. New treatments are also needed for cerebral (late) stage trypanosomiasis. 2,5-Bis(4-amidinophenyl)furan (DB75), a pentamidine analog, has potent in vitro and in vivo anti-trypanosomal activity. However, DB75 does not exhibit significant oral bioavailability and has proved to be ineffective against mouse models of late-stage sleeping sickness regardless of administration route. To circumvent the limited oral bioavailability of DB75, an N-methoxy prodrug 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime (DB289) was designed and developed initially as a compound to treat AIDS-related Pneumocystis carinii pneumonia (PCP). Despite excellent oral activity against early-stage sleeping sickness, oral administration of DB289 exhibited limited efficacy in mouse models of late-stage disease. DB289 has recently entered Phase II(b) clin. trials to treat primary-stage sleeping sickness in Central Africa. The current study takes advantage of the innate fluorescence of DB75 and DB289 along with specific and sensitive quant. analyses to examine plasma and brain distribution of these compds. Animals were dosed with i.v. DB75, oral DB289, and i.v. DB289. Following i.v. administration, DB75 was readily detectable in whole brain exts. and persisted for long periods. Fluorescence microscopy revealed that DB75 did not penetrate into brain parenchyma, however, but was sequestered within cells lining the blood-brain and blood-cerebrospinal fluid barriers. In contrast, brain tissue of mice treated with oral DB289 exhibited diffuse fluorescence within the brain parenchyma, suggesting that the prodrug was not trapped within blood-brain barrier cells (BBB). However, maximal brain concns. of the active compound DB75 were very low (13 nmol/mg of tissue at 24 h). I.v. administration of DB289 resulted in a qual. similar fluorescence pattern to oral DB289, indicating again that DB289 and DB75 were present within brain parenchyma, not only in barrier regions. Furthermore, peak DB75 tissue levels were higher (61 nmol/mg of tissue at 24 h) than with oral prodrug. The near five-fold increase in brain levels of DB289 combined with parenchymal localization of compound fluorescence after i.v. administration suggest that the unaltered prodrug penetrates the blood-brain barrier, and may be subject to in situ biotransformation. I.v. administration of DB289 should be evaluated in mouse models of late-stage sleeping sickness.
IT **73819-26-8**, 2,5-Bis(4-amidinophenyl)furan
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-trypanosomal drug DB75, a pentamidine undetectable in plasma but present for longer time in choroid plexus, meninges due to poor penetration across blood brain barrier after i.v.

intake in mouse)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



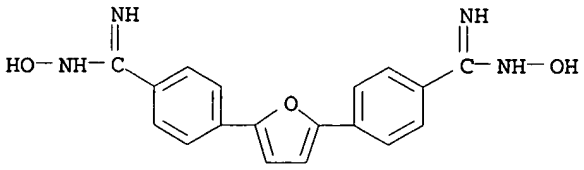
IT **186953-56-0**, 2,5-Bis(4-amidinophenyl)furan-bis-O-methylamidoxime
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral anti-trypanosomal drug DB289 penetrate into brain parenchyma, does not trapped in cells lining brain, but low quantities in brain homogenates, and i.v. administration delivered highest level of active DB75 in mouse)
RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



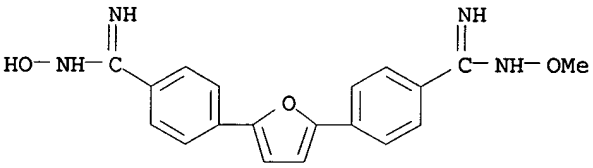
CC 1-5 (Pharmacology)
Section cross-reference(s): 63
IT **Drug delivery** systems
(injections, i.v.; i.v. DB75 do not cross blood-brain barrier but B289 detected in brain parenchyma and i.v. route delivered highest quantity of drug than oral route in mouse and efficacy of i.v. DB289 can be evaluated for African trypanosomiasis)
IT **Drug delivery** systems
(oral; i.v. DB75 do not cross blood-brain barrier but B289 detected in brain parenchyma and i.v. route delivered highest quantity of drug than oral route in mouse and efficacy of i.v. DB289 can be evaluated for African trypanosomiasis)
IT **Drug delivery** systems
(prodrugs; i.v. DB75 do not cross blood-brain barrier but B289 detected in brain parenchyma and i.v. route delivered highest quantity of drug than oral route in mouse and efficacy of i.v. DB289 can be evaluated for African trypanosomiasis)
IT **73819-26-8**, 2,5-Bis(4-amidinophenyl)furan
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-trypanosomal drug DB75, a pentamidine undetectable in plasma but present for longer time in choroid plexus, meninges due to poor penetration across blood brain barrier after i.v. intake in mouse)
IT **186953-56-0**, 2,5-Bis(4-amidinophenyl)furan-bis-O-methylamidoxime
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral anti-trypanosomal drug DB289 penetrate into brain parenchyma, does not trapped in cells lining brain, but low

quantities in brain homogenates, and i.v. administration delivered highest level of active DB75 in mouse)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

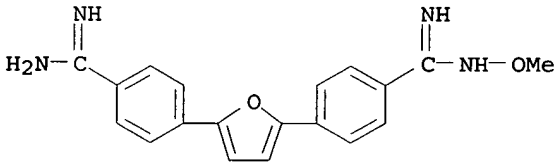
L42 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:336874 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 141:301169
TITLE: Metabolites of an orally active **antimicrobial** prodrug, 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime, identified by liquid chromatography/tandem mass spectrometry
AUTHOR(S): Zhou, Lian; Thakker, Dhiren R.; Voyksner, Robert D.; Anbazhagan, Mariappan; Boykin, David W.; Hall, James E.; Tidwell, Richard R.
CORPORATE SOURCE: Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA
SOURCE: Journal of Mass Spectrometry (2004), 39(4), 351-360
CODEN: JMSPFJ; ISSN: 1076-5174
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB DB75 (2,5-bis(4-amidinophenyl)furan) is a promising **antimicrobial** agent against African trypanosomiasis and Pneumocystis carinii pneumonia. However, it suffers from poor oral activity in rodent models for both infections. In contrast, a novel prodrug of DB75, 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime (DB289), has excellent oral activity. DB289 is currently undergoing clin. investigation as a candidate drug to treat primary stage African trypanosomiasis and Pneumocystis carinii pneumonia. In this study, metabolites of DB289 formed after incubation with freshly isolated rat hepatocytes were characterized using liquid chromatog./ion trap mass spectrometry. Administration of DB289 and octadeuterated DB289 in a 1: 1 mixture greatly facilitated metabolite identification by providing isotope patterns with twin ions separated by 8 m/z units in the ratio 1: 1, in the extracted ion chromatograms of mol. ions and in the product ion mass spectra of metabolites. Ten metabolites were identified. Series of O-demethylations and N-dehydroxylations led to the metabolic activation of DB289 to DB75 with the production of four intermediate phase I metabolites. Phase II glucuronidation and sulfation led to the formation of four glucuronide and one sulfate metabolites.
IT **186953-55-9 475976-08-0 591735-77-2 591736-09-3 761445-94-7 761445-95-8**
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(metabolites of an orally active **antimicrobial** prodrug, 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime, identified by liquid chromatog./tandem mass spectrometry)
RN 186953-55-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



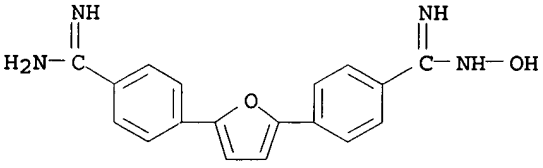
RN 475976-08-0 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



RN 591735-77-2 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)

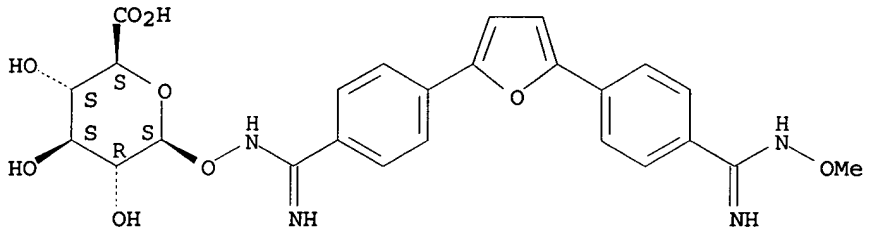


RN 591736-09-3 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-N-hydroxy- (9CI) (CA INDEX NAME)



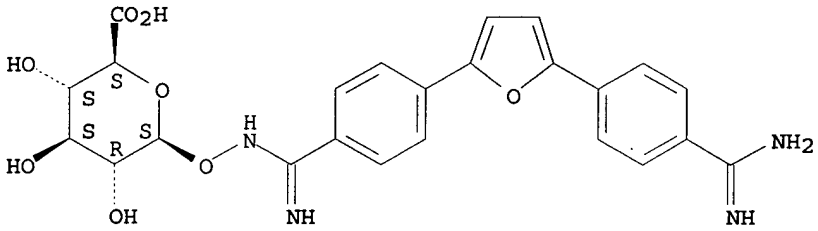
RN 761445-94-7 HCAPLUS
CN β-D-Glucopyranuronic acid, 1-O-[[imino[4-[5-[4-[imino(methoxyamino)methyl]phenyl]-2-furanyl]phenyl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

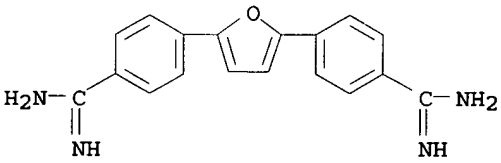


RN 761445-95-8 HCAPLUS
CN β-D-Glucopyranuronic acid, 1-O-[[[4-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]phenyl]iminomethyl]amino]- (9CI) (CA INDEX NAME)

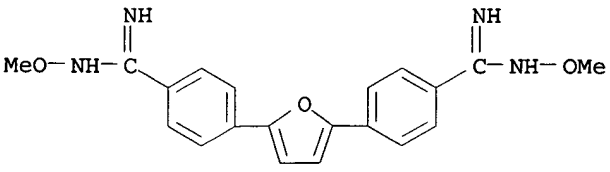
Absolute stereochemistry.



IT **73819-26-8**, DB 75 **186953-56-0**, DB289
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolites of an orally active **antimicrobial** prodrug, 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime, identified by liquid chromatog./tandem mass spectrometry)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



CC 63-5 (Pharmaceuticals)
IT Liver
(hepatocyte; metabolites of an orally active

antimicrobial prodrug, 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime, identified by liquid chromatog./tandem mass spectrometry)

IT Ion trap mass spectrometry
(metabolites of an orally active **antimicrobial** prodrug, 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime, identified by liquid chromatog./tandem mass spectrometry)

IT **Drug delivery** systems
(prodrugs; metabolites of an orally active **antimicrobial** prodrug, 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime, identified by liquid chromatog./tandem mass spectrometry)

IT **186953-55-9 475976-08-0 591735-77-2**
591736-09-3 761445-94-7 761445-95-8
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(metabolites of an orally active **antimicrobial** prodrug, 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime, identified by liquid chromatog./tandem mass spectrometry)

IT **73819-26-8**, DB 75 **186953-56-0**, DB289
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolites of an orally active **antimicrobial** prodrug, 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime, identified by liquid chromatog./tandem mass spectrometry)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 15 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:60255 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 140:105258
TITLE: Benzimidazole compound-pentamidine compound combinations for the treatment of neoplasms
INVENTOR(S): Borisy, Alexis; Keith, Curtis; Foley, Michael A.; Stockwell, Brent R.; Gaw, Debra A.
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006849	A2	20040122	WO 2003-US21984	2003 0715
WO 2004006849	A3	20040603		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-396151P P 2002 0715

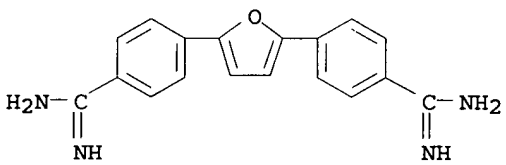
OTHER SOURCE(S): MARPAT 140:105258

AB The invention features a method for treating a patient having a cancer or other neoplasm, by administering to the patient (i) a benzimidazole or a metabolite or analog thereof; and (ii) pentamidine or a metabolite or analog thereof simultaneously or within 14 days of each other in amts. sufficient to inhibit the growth of the neoplasm.

IT **73819-26-8 166601-10-1 166601-11-2 173420-56-9 179118-08-2 179118-22-0 216308-16-6 216308-18-8 247032-11-7 247032-13-9 247032-15-1 247032-16-2 247032-17-3 247032-18-4 442842-45-7 648415-30-9 648415-31-0 648415-32-1 648415-34-3 648415-37-6 648415-38-7 648415-39-8 648415-40-1 648415-41-2 648415-58-1 648415-59-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzimidazole compound-pentamidine compound combinations for the treatment of neoplasms)

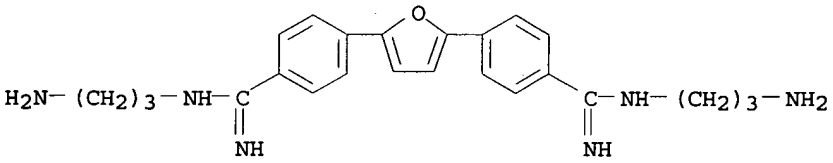
RN 73819-26-8 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



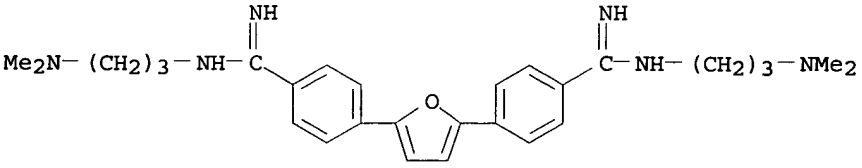
RN 166601-10-1 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(3-aminopropyl)- (9CI) (CA INDEX NAME)



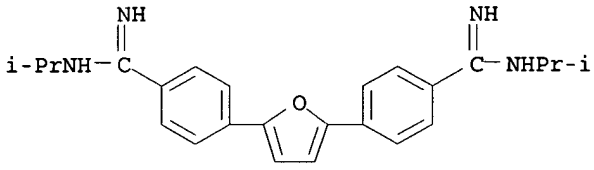
RN 166601-11-2 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)

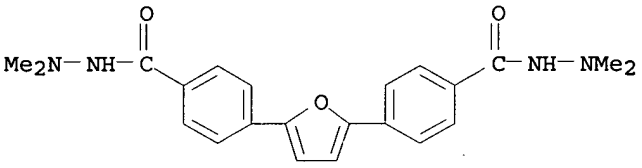


RN 173420-56-9 HCAPLUS

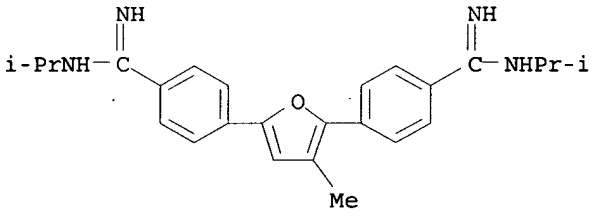
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



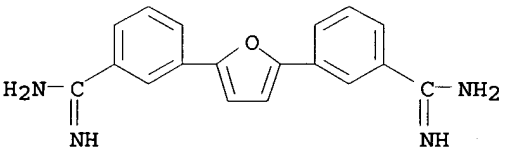
RN 179118-08-2 HCAPLUS
CN Benzoic acid, 4,4'-(2,5-furandiyl)bis-, bis(2,2-dimethylhydrazide) (9CI) (CA INDEX NAME)



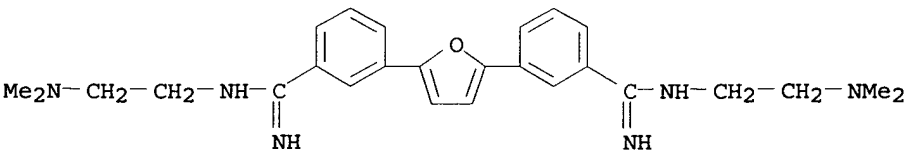
RN 179118-22-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3-methyl-2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 216308-16-6 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)

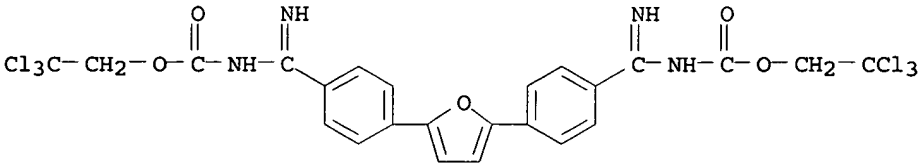


RN 216308-18-8 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis[N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)

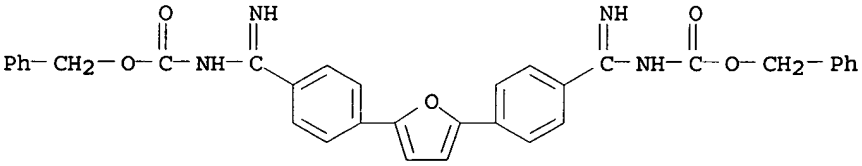


RN 247032-11-7 HCAPLUS

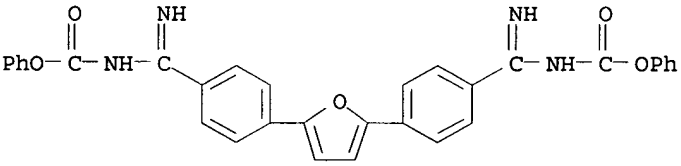
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)



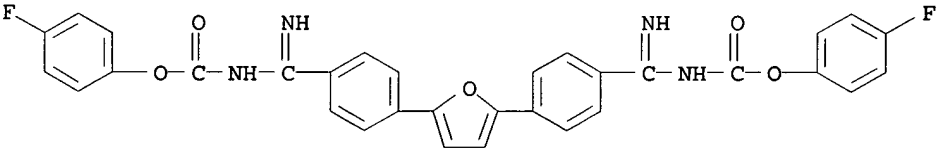
RN 247032-13-9 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



RN 247032-15-1 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, diphenyl ester (9CI) (CA INDEX NAME)

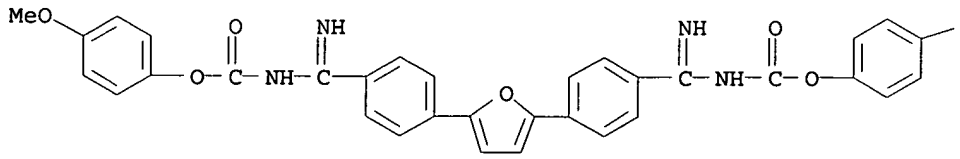


RN 247032-16-2 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-fluorophenyl) ester (9CI) (CA INDEX NAME)



RN 247032-17-3 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-methoxyphenyl) ester (9CI) (CA INDEX NAME)

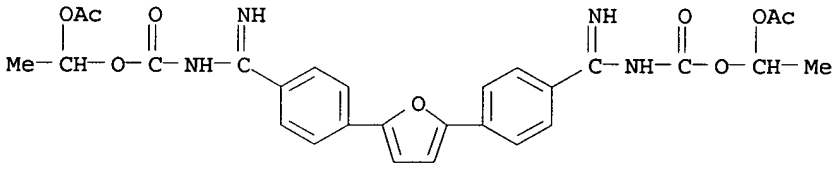
PAGE 1-A



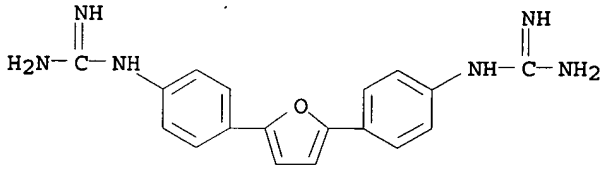
PAGE 1-B

OMe

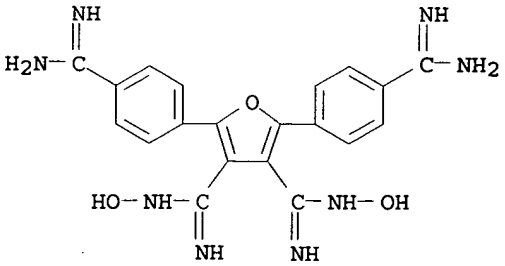
RN 247032-18-4 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis[1-(acetyloxy)ethyl] ester (9CI) (CA INDEX NAME)



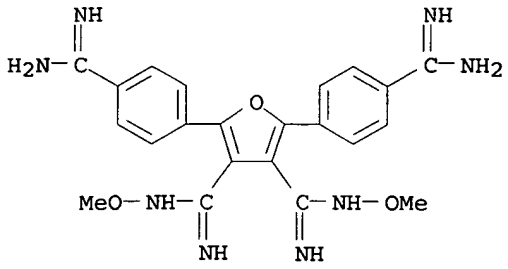
RN 442842-45-7 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis- (9CI) (CA INDEX NAME)



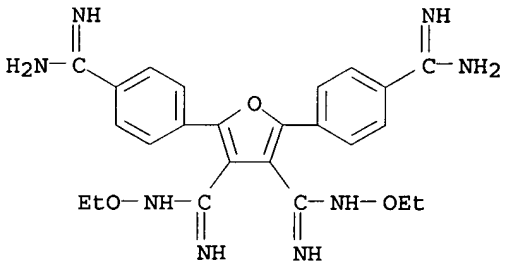
RN 648415-30-9 HCAPLUS
CN 3,4-Furandicarboximidamide, 2,5-bis[4-(aminoiminomethyl)phenyl]-N,N''-dihydroxy- (9CI) (CA INDEX NAME)



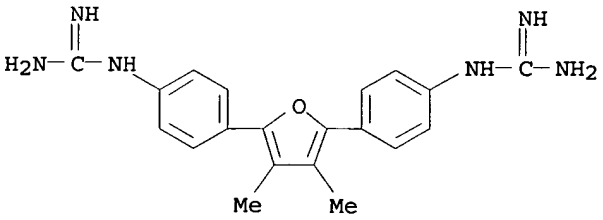
RN 648415-31-0 HCAPLUS
CN 3,4-Furandicarboximidamide, 2,5-bis[4-(aminoiminomethyl)phenyl]-N,N''-dimethoxy- (9CI) (CA INDEX NAME)



RN 648415-32-1 HCAPLUS
CN 3,4-Furandicarboximidamide, 2,5-bis[4-(aminoiminomethyl)phenyl]-N,N''-diethoxy- (9CI) (CA INDEX NAME)



RN 648415-34-3 HCAPLUS
CN Guanidine, N,N'''-[(3,4-dimethyl-2,5-furandiyl)di-4,1-phenylene]bis- (9CI) (CA INDEX NAME)



RN 648415-37-6 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)

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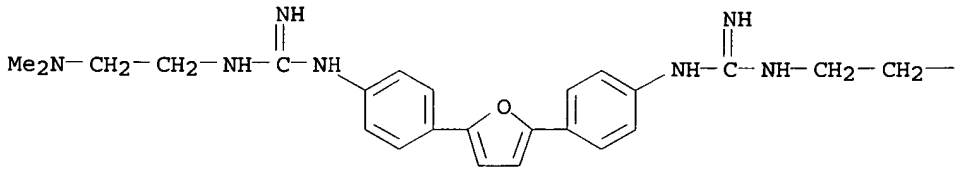
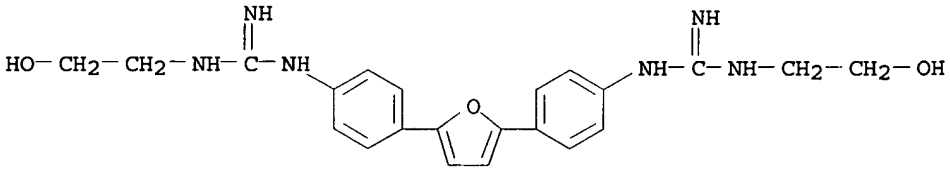


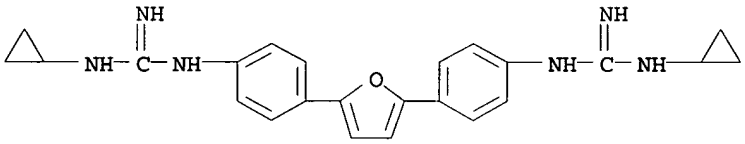
PAGE 1-B

—NMe_2

RN 648415-38-7 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)



RN 648415-39-8 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-cyclopropyl- (9CI) (CA INDEX NAME)



RN 648415-40-1 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-[3-(diethylamino)propyl]- (9CI) (CA INDEX NAME)

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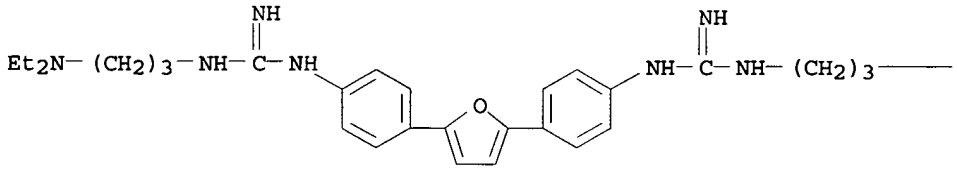
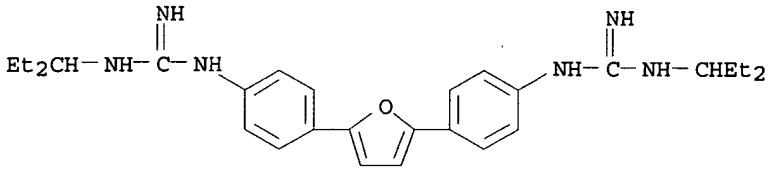


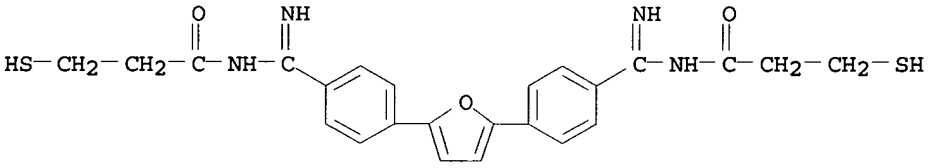
PAGE 1-B

—NEt_2

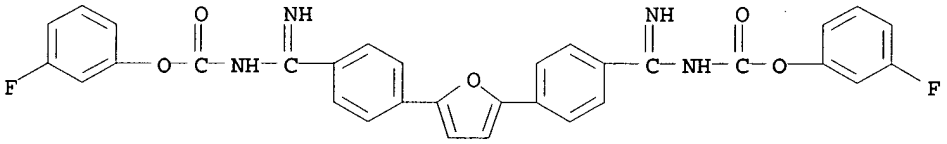
RN 648415-41-2 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-(1-ethylpropyl)- (9CI) (CA INDEX NAME)



RN 648415-58-1 HCAPLUS
CN Propanamide, N,N'-[2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis[3-mercapto- (9CI) (CA INDEX NAME)



RN 648415-59-2 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(3-fluorophenyl) ester (9CI) (CA INDEX NAME)



IC ICM A61K
CC 1-6 (Pharmacology)
IT Antitumor agents
Carcinoma
Drug delivery systems
Drug interactions
Drug screening
Hodgkin's disease
Human
Mammary gland, neoplasm
Melanoma
Neoplasm
Neuroglia, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Polycythemia vera
Prostate gland, neoplasm
Testis, neoplasm
Uterus, neoplasm
(benzimidazole compound-pentamidine compound combinations for the treatment of neoplasms)
IT **Drug delivery** systems
(inhalants; benzimidazole compound-pentamidine compound combinations for the treatment of neoplasms)
IT **Drug delivery** systems
(injections, i.m.; benzimidazole compound-pentamidine compound combinations for the treatment of neoplasms)
IT **Drug delivery** systems
(injections, i.v.; benzimidazole compound-pentamidine compound

combinations for the treatment of neoplasms)
IT **Drug delivery** systems
(oral; benzimidazole compound-pentamidine compound combinations for the treatment of neoplasms)
IT **Drug delivery** systems
(rectal; benzimidazole compound-pentamidine compound combinations for the treatment of neoplasms)
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648415-59-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzimidazole compound-pentamidine compound combinations for the treatment of neoplasms)

L42 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:60249 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 140:122767
TITLE: Pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms
INVENTOR(S): Borisy, Alexis; Keith, Curtis; Foley, Michael A.; Stockwell, Brent R.; Gaw, Debra A.; Nichols, M. James; Lee, Margaret S.
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006842	A2	20040122	WO 2003-US21803	2003 0711
WO 2004006842	A3	20040527		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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JP 2005536509	T2	20051202	JP 2004-521730	2003 0711
NO 2005000204	A	20050408	NO 2005-204	2005 0113

PRIORITY APPLN. INFO.: US 2002-395233P P 2002 0711

WO 2003-US21803 W
2003
0711

OTHER SOURCE(S): MARPAT 140:122767

AB The invention features a method for treating a patient having a cancer or other neoplasm by administering to the patient pentamidine (or an analog thereof) and chlorpromazine (or an analog thereof) simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

IT **73819-26-8 73819-28-0 166601-10-1**
166601-11-2 173420-56-9 179118-08-2
179118-22-0 216308-16-6 216308-18-8
247032-11-7 247032-13-9 247032-15-1
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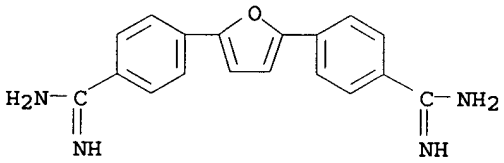
648417-91-8 648417-95-2 648417-98-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms)

RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



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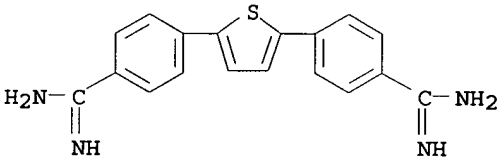

RN 166601-10-1 HCAPLUS
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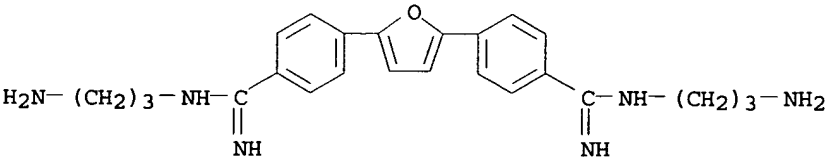

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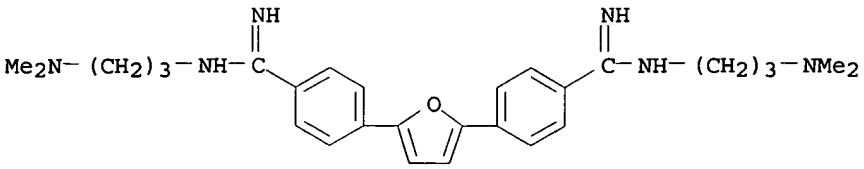
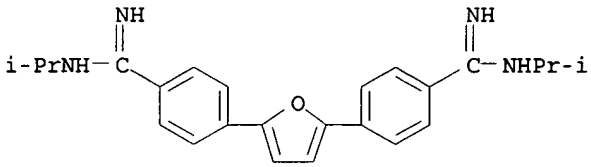
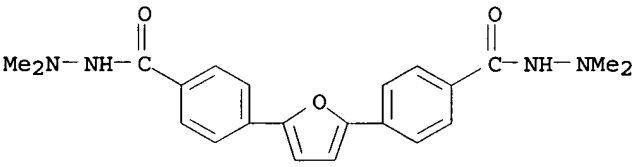


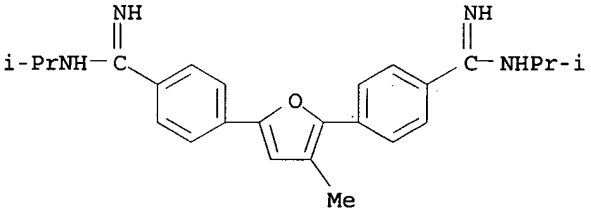
RN 173420-56-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)-(9CI) (CA INDEX NAME)



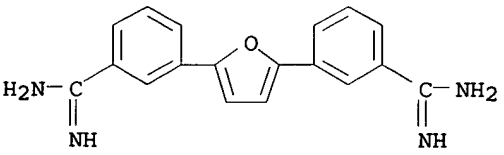
RN 179118-08-2 HCAPLUS
CN Benzoic acid, 4,4'-(2,5-furandiyl)bis-, bis(2,2-dimethylhydrazide) (9CI) (CA INDEX NAME)



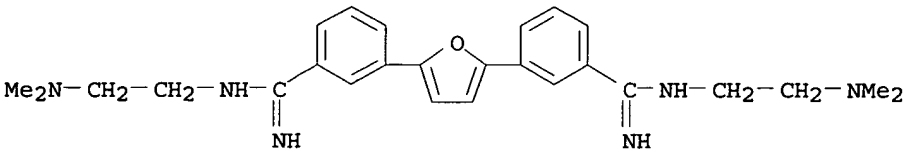
RN 179118-22-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3-methyl-2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



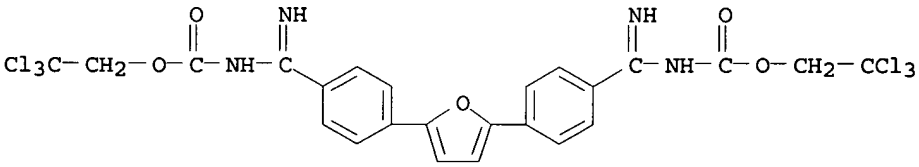
RN 216308-16-6 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



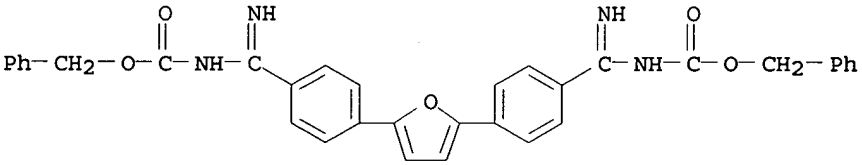
RN 216308-18-8 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis[N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



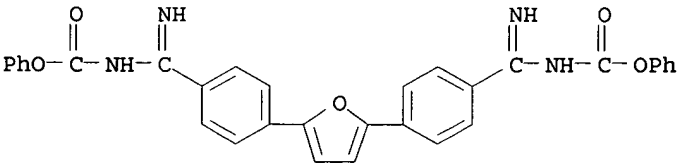
RN 247032-11-7 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)



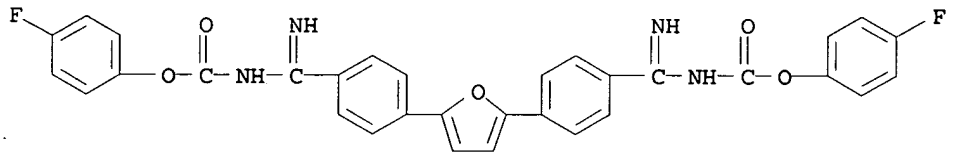
RN 247032-13-9 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)



RN 247032-15-1 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, diphenyl ester (9CI) (CA INDEX NAME)



RN 247032-16-2 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-fluorophenyl) ester (9CI) (CA INDEX NAME)



RN 247032-17-3 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-methoxyphenyl) ester (9CI) (CA INDEX NAME)

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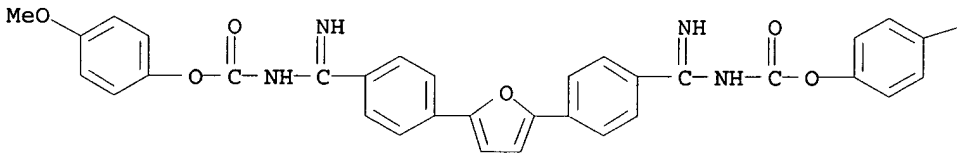
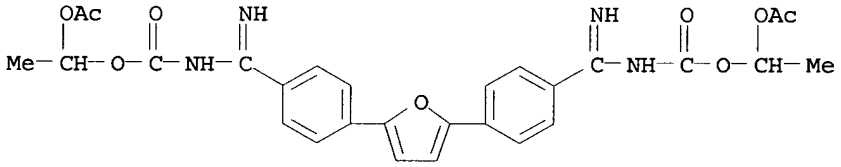


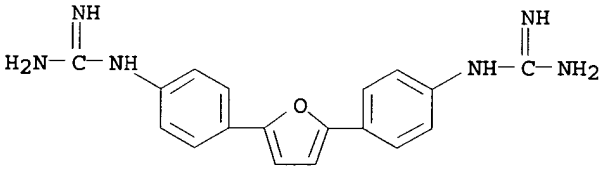
PAGE 1-B

OMe

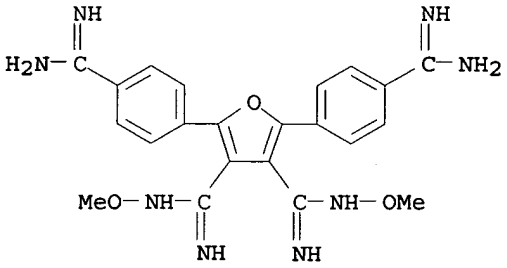
RN 247032-18-4 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis[1-(acetyloxy)ethyl] ester (9CI) (CA INDEX NAME)



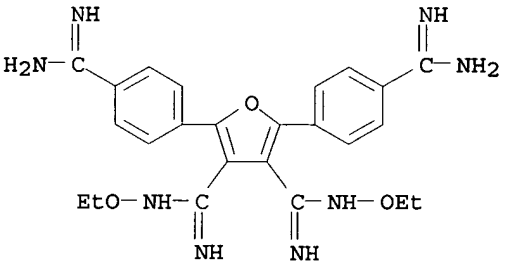
RN 442842-45-7 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis- (9CI) (CA INDEX NAME)



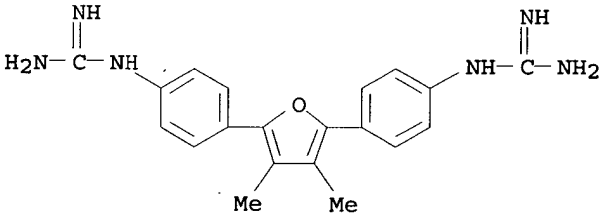
RN 648415-31-0 HCAPLUS
CN 3,4-Furandicarboximidamide, 2,5-bis[4-(aminoiminomethyl)phenyl]-N,N''-dimethoxy- (9CI) (CA INDEX NAME)



RN 648415-32-1 HCAPLUS
CN 3,4-Furandicarboximidamide, 2,5-bis[4-(aminoiminomethyl)phenyl]-N,N''-diethoxy- (9CI) (CA INDEX NAME)



RN 648415-34-3 HCAPLUS
CN Guanidine, N,N'''-[(3,4-dimethyl-2,5-furandiyl)di-4,1-phenylene]bis- (9CI) (CA INDEX NAME)



RN 648415-37-6 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)

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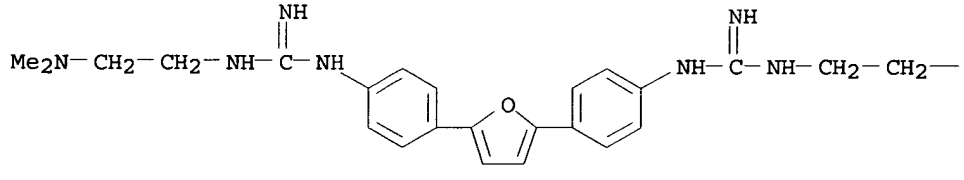
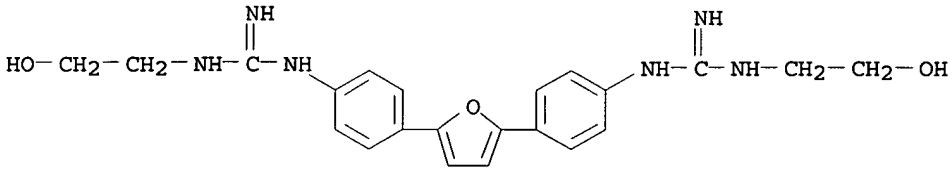


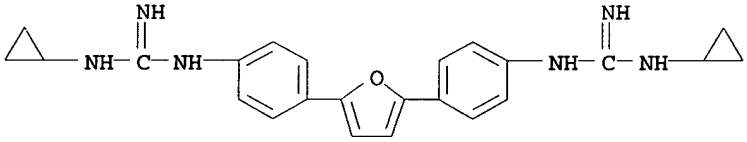
PAGE 1-B

—NMe_2

RN 648415-38-7 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

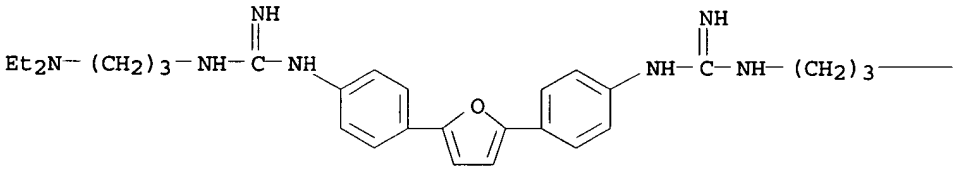


RN 648415-39-8 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-cyclopropyl- (9CI) (CA INDEX NAME)



RN 648415-40-1 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-[3-(diethylamino)propyl]- (9CI) (CA INDEX NAME)

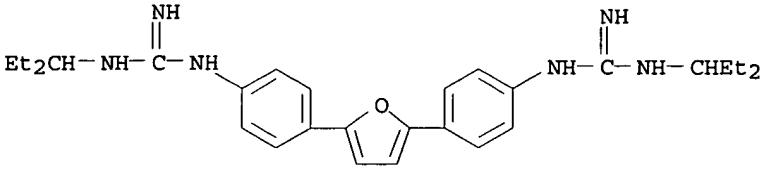
PAGE 1-A



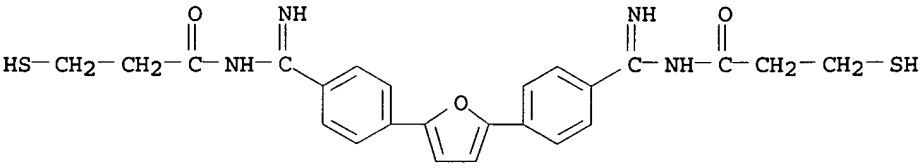
PAGE 1-B

—NEt_2

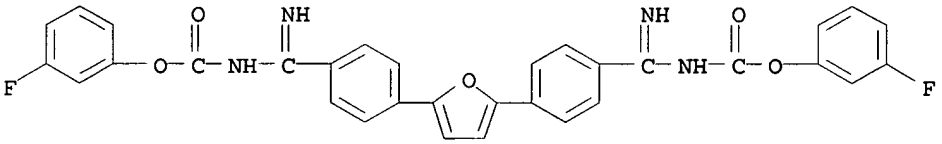
RN 648415-41-2 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis[N'-(1-ethylpropyl)- (9CI) (CA INDEX NAME)



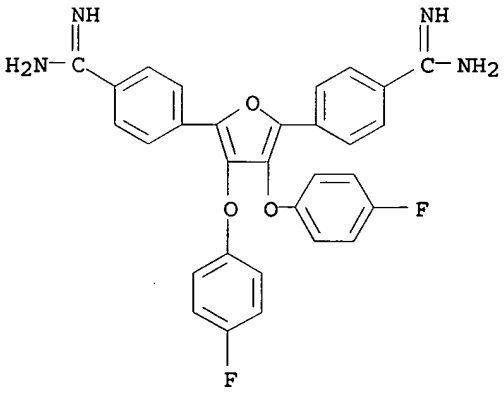
RN 648415-58-1 HCAPLUS
CN Propanamide, N,N'-[2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis[3-mercapto- (9CI) (CA INDEX NAME)



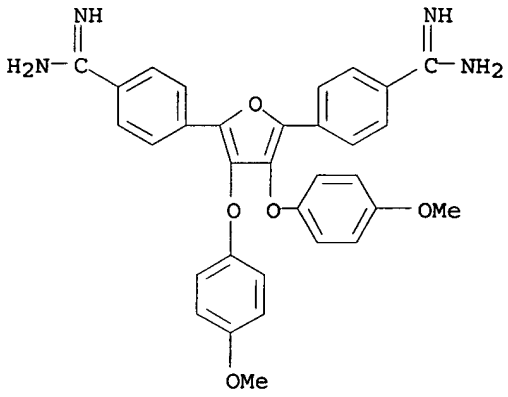
RN 648415-59-2 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(3-fluorophenyl) ester (9CI) (CA INDEX NAME)



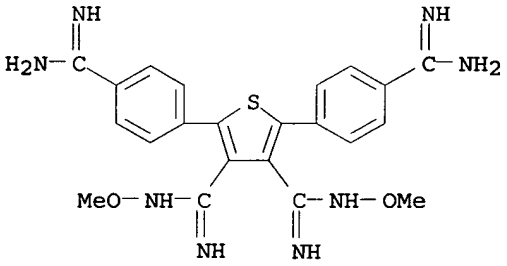
RN 648417-90-7 HCAPLUS
CN Benzenecarboximidamide, 4,4'-[3,4-bis(4-fluorophenoxy)-2,5-furandiyl]bis- (9CI) (CA INDEX NAME)



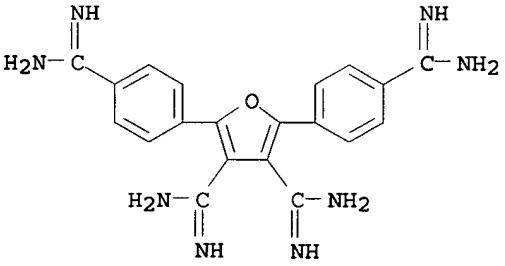
RN 648417-91-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-[3,4-bis(4-methoxyphenoxy)-2,5-furandiyl]bis- (9CI) (CA INDEX NAME)



RN 648417-95-2 HCAPLUS
CN 3,4-Thiophenedicarboximidamide, 2,5-bis[4-(aminoiminomethyl)phenyl]-N,N''-dimethoxy- (9CI) (CA INDEX NAME)



RN 648417-98-5 HCAPLUS
CN 3,4-Furandicarboximidamide, 2,5-bis[4-(aminoiminomethyl)phenyl]- (9CI) (CA INDEX NAME)



IC ICM A61K
CC 1-6 (Pharmacology)
IT **Drug delivery** systems
(inhalants; pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms)
IT **Drug delivery** systems
(injections, i.m.; pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms)
IT **Drug delivery** systems
(injections, i.v.; pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms)
IT **Drug delivery** systems
(oral; pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms)

IT Angiogenesis inhibitors
Antitumor agents
Carcinoma
Chemotherapy
Cytotoxic agents
Drug delivery systems
Drug interactions
Gene therapy
Hodgkin's disease
Human
Immunotherapy
Lung, neoplasm
Mammary gland, neoplasm
Melanoma
Neoplasm
Neuroglia, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Polycythemia vera
Prostate gland, neoplasm
Radiotherapy
Surgery
Testis, neoplasm
Uterus, neoplasm
(pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms)

IT **Drug delivery** systems
(rectal; pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms)

IT 50-18-0, Cyclophosphamide 50-44-2, Mercaptopurine 50-52-2, Thioridazine 50-53-3D, Chlorpromazine, analogs 51-21-8, 5-Fluorouracil 57-22-7, Vincristine 58-38-8, Prochlorperazine 58-39-9, Perphenazine 59-05-2, Methotrexate 60-87-7, Promethazine 60-89-9, Mepazine 60-99-1, Methotrimeprazine 61-01-8, Methoxypromazine 69-23-8, Fluphenazine 84-06-0, Thiopropazate 84-97-9, Perazine 100-33-4, Pentamidine 100-33-4D, Pentamidine, analogs 101-62-2, Phenamidine 104-32-5, Propamidine 117-89-5, Trifluoperazine 122-06-5, Stilbamidine 146-54-3, Triflupromazine 148-82-3, Melphalan 154-93-8, Carmustine 305-03-3, Chlorambucil 362-29-8, Propiomazine 495-99-8, Hydroxystilbamidine 496-00-4, Dibrompropamidine 536-71-0, Diminazene 548-04-9, Hypericin 566-48-3, Formestane 618-39-3, Benzamidine 653-03-2, Butaperazine 865-21-4, Vinblastine 1225-64-5, Norchlorpromazine 1402-38-6, Actinomycin 1404-00-8, Mitomycin 1420-55-9, Thiethylperazine 1438-30-8, Netropsin 2095-24-1, Chlorfenethazine 3459-96-9, Amicarbalide 3546-03-0, Cyamemazine 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 13311-84-7, Flutamide 15663-27-1, Cisplatin 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 33419-42-0, Etoposide 33763-36-9, 3,7-Dibenzofurandicarbonitrile 39389-47-4, Distamycin 41738-62-9, 3,7-Dibenzothiophenedicarbonitrile 41738-64-1, 3,7-Dibenzothiophenediamine 53714-56-0, Leuprorelin 56420-45-2, Epirubicin 63612-50-0, Nilutamide 65807-02-5, Goserelin 66639-24-5 67019-91-4 71486-22-1, Vinorelbine **73819-26-8 73819-28-0** 74733-75-8 75846-15-0 75846-16-1 80498-71-1 80498-74-4 83834-10-0 89778-26-7 90357-06-5, Bicalutamide 91371-12-9 94345-47-8, Heptamidine 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 100562-53-6 101689-95-6 107868-30-4, Exemestane 112809-51-5, Letrozole 112887-68-0, Raltitrexed 114977-28-5, Docetaxel 120511-73-1, Anastrozole 123948-87-8, Topotecan 124076-61-5, Butamidine 124076-65-9 148344-21-2 154361-50-9, Capecitabine 157168-41-7 157168-42-8 157168-43-9 157168-44-0 157168-45-1 157168-46-2 157168-47-3 157168-48-4

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648415-36-5 **648415-37-6 648415-38-7**
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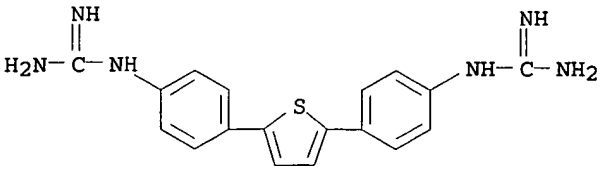
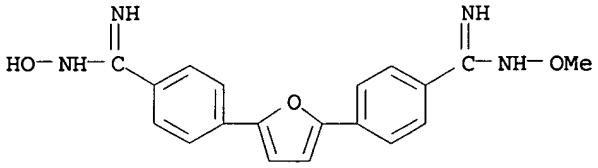
648417-92-9 648417-93-0 648417-94-1 **648417-95-2**
648417-96-3 648417-97-4 **648417-98-5** 648418-01-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pentamidine compound-chlorpromazine compound combinations for the treatment of neoplasms)

L42 ANSWER 17 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:831312 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 141:225237
TITLE: Part i. synthesis of n-substituted 2,5-bis-[4-guanidinophenyl]thiophenes as potential antileishmanial compounds. part ii. synthesis of novel potential prodrugs of bis-guanidino and bis-amidino molecules
AUTHOR(S): Gonzalez-Roman, Jose Luis
CORPORATE SOURCE: Georgia State Univ., Experiment, GA, USA
SOURCE: (2002) 95 pp. Avail.: UMI, Order No. DA3075422
From: Diss. Abstr. Int., B 2003, 63(12), 5849
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **423165-31-5DP**, derivative
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of N-substituted 2,5-bis-[4-guanidinophenyl]thiophenes as potential antileishmanial compds.)
RN 423165-31-5 HCAPLUS
CN Guanidine, N,N'''-(2,5-thiophenediyldi-4,1-phenylene)bis- (9CI) (CA INDEX NAME)

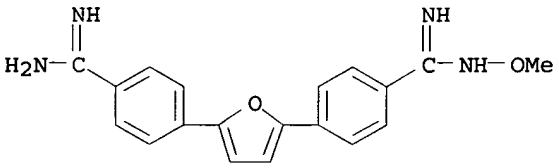


CC 27-8 (Heterocyclic Compounds (One Hetero Atom))
IT **Drug delivery** systems
(prodrugs; synthesis of novel potential prodrugs of bis-guanidino and bis-amidino mols.)
IT **423165-31-5DP**, derivative
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of N-substituted 2,5-bis-[4-guanidinophenyl]thiophenes as potential antileishmanial compds.)

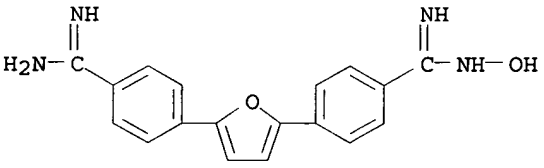
L42 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:338839 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 139:230527
TITLE: Synthesis of metabolites of the prodrug 2,5-bis(4-o-methoxyamidinophenyl)furan
AUTHOR(S): Anbazhagan, Mariappan; Saulter, Janelle Y.; Hall, James E.; Boykin, David W.
CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Heterocycles (2003), 60(5), 1133-1145
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:230527
AB The synthesis of three metabolites of the prodrug 2,5-bis(4-O-methoxyamidinophenyl)furan [i.e., 4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide]] was reported. Metabolites included 4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxybenzenecarboximidamide, 4-[5-[4-[(methoxyamino)iminomethyl]phenyl]-2-furanyl]benzenecarboximidamide and 4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]benzenecarboximidamide. The key step in each of the syntheses involves the Heck reaction.
IT **475976-08-0P**, 4-[5-[4-[(Hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxybenzenecarboximidamide **591735-77-2P**, 4-[5-[4-[(Methoxyamino)iminomethyl]phenyl]-2-furanyl]benzenecarboximidamide **591736-09-3P**, 4-[5-[4-[(Hydroxyamino)iminomethyl]phenyl]-2-furanyl]benzenecarboximidamide
RL: SPN (Synthetic preparation); PREP (Preparation)
(4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide] metabolite; preparation of metabolites of prodrug [4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide])
RN 475976-08-0 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



RN 591735-77-2 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)

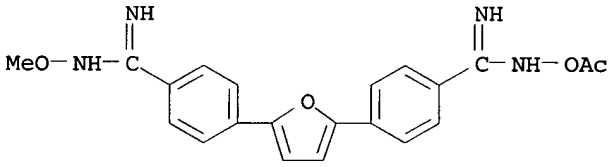


RN 591736-09-3 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-N-hydroxy- (9CI) (CA INDEX NAME)

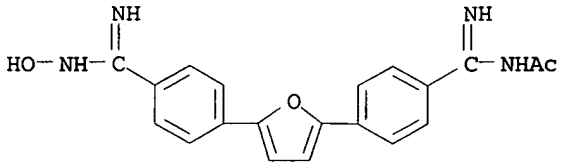


IT **591735-85-2P 591735-99-8P 591736-07-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of metabolites of prodrug [4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide])

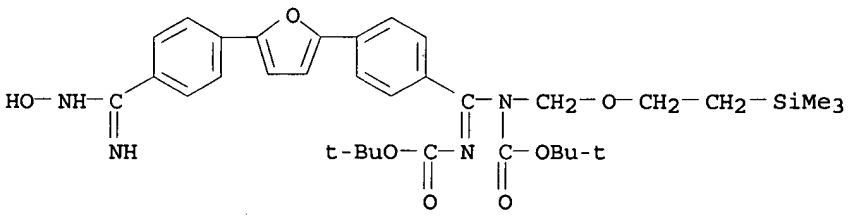
RN 591735-85-2 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-[[(acetyloxy)amino]iminomethyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



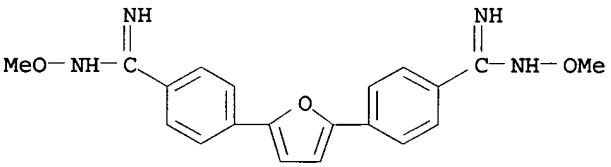
RN 591735-99-8 HCAPLUS
CN Acetamide, N-[[4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]phenyl]iminomethyl]- (9CI) (CA INDEX NAME)



RN 591736-07-1 HCAPLUS
CN 6-Oxa-2,4-diaza-9-siladec-2-enoic acid, 4-[(1,1-dimethylethoxy)carbonyl]-3-[4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]phenyl]-9,9-dimethyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT **186953-56-0DP**, 4,4'-(2,5-Furandiyl)bis[N-methoxybenzenecarboximidamide], metabolites
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of metabolites of prodrug [4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide])
RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



CC 27-6 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 63
ST hydroxyaminoiminomethylphenyl furanyl benzenecarboximidamide metabolite prepn; methoxyaminoiminomethylphenyl furanyl benzenecarboximidamide metabolite prepn; methoxyamidinophenyl furan metabolite prodrug prepn; aminoiminomethylphenyl furanyl benzenecarboximidamide metabolite prepn; **drug delivery** prodrug aminoiminomethylphenyl furanyl benzenecarboximidamide metabolite prepn; prodrug aminoiminomethylphenyl furanyl benzenecarboximidamide metabolite prepn
IT **Drug delivery** systems
(prodrugs; preparation of metabolites of prodrug [4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide])
IT **475976-08-0P**, 4-[5-[4-[(Hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxybenzenecarboximidamide **591735-77-2P**, 4-[5-[4-[(Methoxyamino)iminomethyl]phenyl]-2-furanyl]benzenecarboximidamide **591736-09-3P**, 4-[5-[4-[(Hydroxyamino)iminomethyl]phenyl]-2-furanyl]benzenecarboximidamide

RL: SPN (Synthetic preparation); PREP (Preparation)
(4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide] metabolite; preparation of metabolites of prodrug [4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide])

IT 591735-79-4P, 4-(2-Furanyl)-N-hydroxybenzenecarboxamidamide 591735-81-8P 591735-83-0P **591735-85-2P** 591735-87-4P, 4-(2-Furanyl)benzenecarboxamidamide 591735-89-6P 591735-91-0P 591735-93-2P 591735-95-4P 591735-97-6P **591735-99-8P** 591736-03-7P 591736-05-9P **591736-07-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of metabolites of prodrug [4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide])

IT **186953-56-0DP**, 4,4'-(2,5-Furandiyl)bis[N-methoxybenzenecarboximidamide], metabolites
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of metabolites of prodrug [4,4'-(2,5-furandiyl)bis[N-methoxybenzenecarboximidamide])

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:173414 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 138:215350
TITLE: Amidine derivatives for treating amyloid-related diseases
INVENTOR(S): Chalifour, Robert J.; Kong, Xianqi; Wu, Xinfu; Lu, Wenshuo
PATENT ASSIGNEE(S): Neurochem Inc., Can.
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003017994	A1	20030306	WO 2002-CA1353	20020903
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2455497	AA	20030306	CA 2002-2455497	20020903
US 2004006092	A1	20040108	US 2002-234643	20020903
EP 1420773	A1	20040526	EP 2002-758012	20020903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

BR 2002012078	A	20040928	BR 2002-12078	2002 0903
JP 2005504053	T2	20050210	JP 2003-522514	2002 0903
US 2004147531	A1	20040729	US 2003-731463	2003 1205
NO 2004000497	A	20040414	NO 2004-497	2004 0204
PRIORITY APPLN. INFO.:			US 2001-316761P	P 2001 0831
			US 2002-387001P	P 2002 0607
			US 2002-234643	A1 2002 0903
			WO 2002-CA1353	W 2002 0903

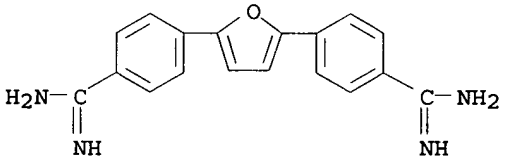
OTHER SOURCE(S): MARPAT 138:215350

AB The invention discloses the use of amidine compds. in the treatment of amyloid-related diseases (e.g. Alzheimer's disease, Down's syndrome, type II diabetes). In particular, the invention discloses a method for treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amount of an amidine compound The compds. of the invention (Markush included) are such that, when administered, reduce or inhibit amyloid fibril formation, neurodegeneration, or cellular toxicity. Compound preparation is described.

IT **73819-26-8 80498-65-3 173420-56-9 179118-06-0 186953-56-0 500714-86-3 500714-90-9 500714-96-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amidine derivs. for treating amyloid-related diseases)

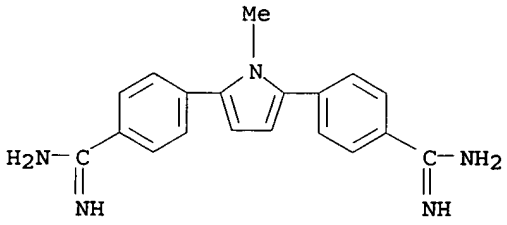
RN 73819-26-8 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)

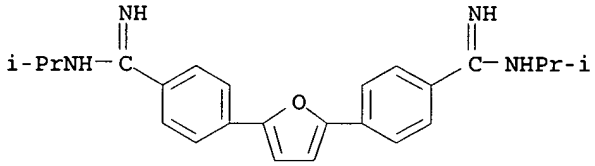


RN 80498-65-3 HCAPLUS

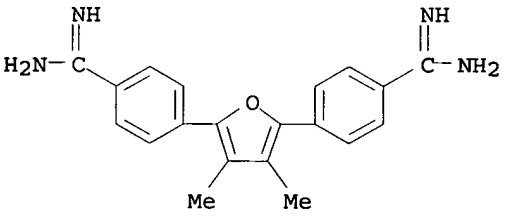
CN Benzenecarboximidamide, 4,4'-(1-methyl-1H-pyrrole-2,5-diyl)bis- (9CI) (CA INDEX NAME)



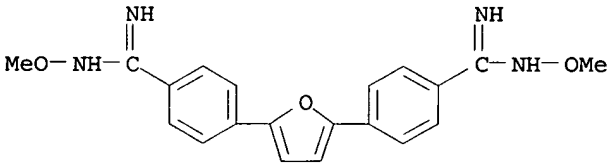
RN 173420-56-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



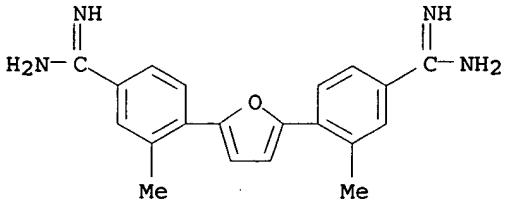
RN 179118-06-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3,4-dimethyl-2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



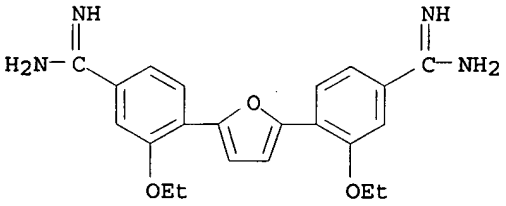
RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



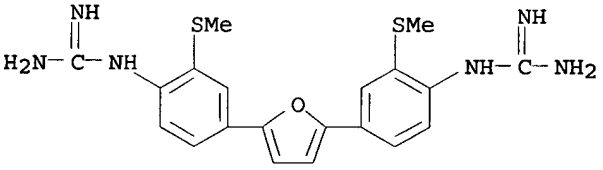
RN 500714-86-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[3-methyl- (9CI) (CA INDEX NAME)



RN 500714-90-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[3-ethoxy- (9CI) (CA INDEX NAME)



RN 500714-96-5 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis[2-(methylthio)-4,1-phenylene]]bis- (9CI) (CA INDEX NAME)



IC ICM A61K031-155
CC 1-12 (Pharmacology)
Section cross-reference(s): 25, 28
IT Alzheimer's disease
Anti-Alzheimer's agents
Antidiabetic agents
Cognition
Cognition enhancers
Cognitive disorders
Cytoprotective agents
Cytotoxicity
Down's syndrome
Drug delivery systems
Human
(amidine derivs. for treating amyloid-related diseases)
IT 100-33-4 140-64-7 1670-14-0 2498-50-2 22265-37-8
26130-55-2 28718-90-3 29148-07-0 34415-16-2 50357-53-4
50357-58-9 53657-95-7 53657-96-8 53733-05-4 56406-50-9
56806-77-0 57928-60-6 59855-11-7 66639-09-6 66639-21-2
67833-70-9 67833-74-3 71889-77-5, 5-Benzofurancarboximidamide
73819-26-8 74938-88-8 77838-86-9 77838-95-0
80498-65-3 99800-90-5 100562-51-4 109444-03-3
118531-15-0 125880-53-7 125880-64-0 129051-01-0
147125-43-7 148344-27-8 152294-33-2 152294-34-3
160522-87-2 163228-14-6 163228-15-7 163228-23-7
167569-14-4 **173420-56-9** 174912-15-3

179118-06-0 186395-26-6 **186953-56-0**
200205-81-8 200878-42-8 204589-04-8 206532-34-5
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433735-87-6 433735-89-8 500713-38-2 500713-42-8
500713-45-1 500713-52-0 500713-56-4 500713-59-7
500713-61-1 500713-63-3 500713-65-5 500713-68-8
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500714-02-3 500714-04-5 500714-06-7 500714-08-9
500714-21-6 500714-23-8 500714-29-4 500714-31-8
500714-34-1 500714-40-9 500714-42-1 500714-44-3
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500714-79-4 500714-81-8 500714-83-0 **500714-86-3**
500714-88-5 **500714-90-9** 500714-91-0 500714-92-1
500714-93-2 500714-94-3 500714-95-4 **500714-96-5**
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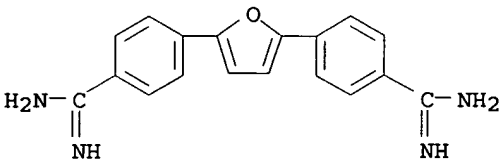
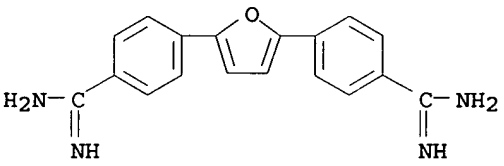
500715-46-8 500715-47-9 500715-48-0 500715-49-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amidine derivs. for treating amyloid-related diseases)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 20 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:70144 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 138:265016
TITLE: **Antimicrobial** activity of the DNA minor groove binders furamidine and analogs
AUTHOR(S): Boykin, David W.
CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303-3088, USA
SOURCE: Journal of the Brazilian Chemical Society (2002), 13(6), 763-771
CODEN: JOCSET; ISSN: 0103-5053
PUBLISHER: Sociedade Brasileira de Quimica
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Aryl diamidine analogs of pentamidine and berenil that bind to the minor groove of DNA have been developed which show broad spectrum **antimicrobial** activity. Several series of analogs of 2,5-bis[4-amidinophenyl]furan (furamidine) have been described which are quite effective when given i.v., however they are ineffective on oral administration. Amidoxime and carbamate prodrugs of furamidine are quite effective when given orally. One of these prodrugs, a bis-O-methylamidoxime is currently in Phase II clin. trials.
IT **73819-26-8**, Furamidine **73819-26-8D**, Furamidine, analogs
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antimicrobial** activity of DNA minor groove binders)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)

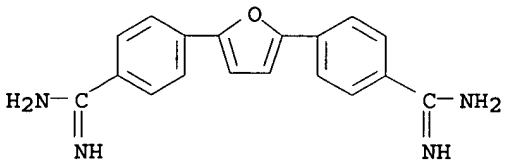


RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)

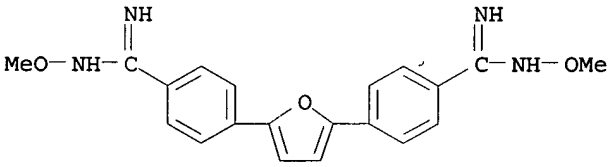


CC 1-0 (Pharmacology)
ST review **antimicrobial** DNA minor groove binder furamidine analog
IT **Antimicrobial** agents
(DNA minor groove binders furamidine and analogs as)
IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**antimicrobial** activity of DNA minor groove binders)
IT **73819-26-8**, Furamidine **73819-26-8D**, Furamidine, analogs
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antimicrobial** activity of DNA minor groove binders)
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:920331 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 138:265107
TITLE: Mechanisms for absorption and metabolism of 2,5-bis(4-amidinophenyl)furan-bis-o-methylamidoxime, an orally active prodrug of the **antimicrobial** agent 2,5-bis(4-amidinophenyl)furan
AUTHOR(S): Zhou, Lian
CORPORATE SOURCE: Univ. of North Carolina, Chapel Hill, NC, USA
SOURCE: (2002) 199 pp. Avail.: UMI, Order No. DA3047101
From: Diss. Abstr. Int., B 2002, 63(3), 1295
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **73819-26-8**, DB 75
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(DB 75; mechanisms for absorption and metabolism of 2,5-bis(4-amidinophenyl)furan- bis-o-methylamidoxime, an orally active prodrug of the **antimicrobial** agent 2,5-bis(4-amidinophenyl)furan)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



IT **186953-56-0**, DB289
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(mechanisms for absorption and metabolism of 2,5-bis(4-amidinophenyl)furan- bis-o-methylamidoxime, an orally active prodrug of the **antimicrobial** agent 2,5-bis(4-amidinophenyl)furan)
RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



CC 1-2 (Pharmacology)
Section cross-reference(s): 63
IT **Antimicrobial** agents
(mechanisms for absorption and metabolism of 2,5-bis(4-amidinophenyl)furan- bis-o-methylamidoxime, an orally active prodrug of the **antimicrobial** agent 2,5-bis(4-amidinophenyl)furan)
IT **Drug delivery** systems
(prodrugs; mechanisms for absorption and metabolism of 2,5-bis(4-amidinophenyl)furan- bis-o-methylamidoxime, an orally active prodrug of the **antimicrobial** agent 2,5-bis(4-amidinophenyl)furan)
IT Biological transport
(uptake; mechanisms for absorption and metabolism of 2,5-bis(4-amidinophenyl)furan- bis-o-methylamidoxime, an orally active prodrug of the **antimicrobial** agent 2,5-bis(4-amidinophenyl)furan)
IT **73819-26-8**, DB 75
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(DB 75; mechanisms for absorption and metabolism of 2,5-bis(4-amidinophenyl)furan- bis-o-methylamidoxime, an orally active prodrug of the **antimicrobial** agent 2,5-bis(4-amidinophenyl)furan)
IT **186953-56-0**, DB289
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(mechanisms for absorption and metabolism of 2,5-bis(4-amidinophenyl)furan- bis-o-methylamidoxime, an orally active prodrug of the **antimicrobial** agent 2,5-bis(4-amidinophenyl)furan)

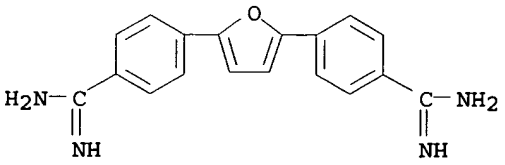
L42 ANSWER 22 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:809292 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 139:90233
TITLE: Enhanced Permeability of the **Antimicrobial** Agent 2,5-Bis(4-Amidinophenyl)Furan Across Caco-2 Cell Monolayers Via Its Methylamidoxime Prodrug

AUTHOR(S): Zhou, Lian; Lee, Kiho; Thakker, Dhiren R.; Boykin, David W.; Tidwell, Richard R.; Hall, James E.
CORPORATE SOURCE: Division of Medicinal Chemistry and Natural Products, Georgia State Univ., Atlanta, GA, 30303, USA
SOURCE: Pharmaceutical Research (2002), 19(11), 1689-1695
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

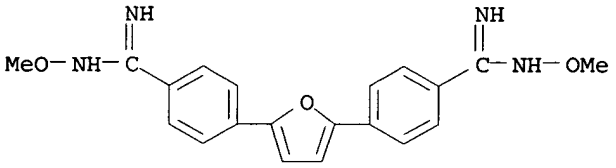
AB Purpose. DB75 [2,5-bis(4-amidinophenyl)furan] is a promising **antimicrobial** agent although it has poor oral potency. In contrast, its novel prodrug, 2,5-bis(4-amidinophenyl)furan-bis-O-methyl- amidoxime (DB289), has excellent oral potency. The mechanisms of transport of DB289 and DB75 across intestinal epithelium have been investigated in these studies to understand differences in their oral potency. Methods. Caco-2 cell monolayers were used as an in vitro model to examine the mechanisms of transport of DB289 and DB75. Samples collected from the transport studies were quantified using high-performance liquid chromatog. with UV and fluorescence detection. Results. A low permeability coefficient (3.8 + 10-7 cm/s for transport in apical [AP] to basolateral [BL] direction) and high sensitivity to extracellular Ca2+ suggest that AP to BL transport of DB75 across Caco-2 cell monolayers occurs predominantly via a paracellular route. DB289 has an 85-fold higher transport rate (322.0 + 10-7 cm/s for transport in the AP to BL direction) across Caco-2 monolayers than that of DB75. This, with its insensitivity to extracellular Ca2+ indicates that AP to BL transport of DB289 across Caco-2 cell monolayers occurs predominantly via a transcellular route. Conclusions. DB75 is transported across Caco-2 cell monolayers predominantly via paracellular pathways, whereas the prodrug DB289 is transported via transcellular pathways. This could account for the much higher oral activity of DB289 over DB75.

IT **73819-26-8**, DB 75 **186953-56-0**, DB289
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of transport of **antimicrobial** bis(amidinophenyl)furan and its prodrug across intestinal epithelium)

RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 2
ST intestine transport **antimicrobial** amidinophenyl furan prodrug
IT Animal cell line
(Caco-2; mechanisms of transport of **antimicrobial** bis(amidinophenyl)furan and its prodrug across intestinal epithelium)
IT Biological transport
(drug; mechanisms of transport of **antimicrobial** bis(amidinophenyl)furan and its prodrug across intestinal epithelium)
IT Intestine
(epithelium; mechanisms of transport of **antimicrobial** bis(amidinophenyl)furan and its prodrug across intestinal epithelium)
IT Epithelium
(intestinal; mechanisms of transport of **antimicrobial** bis(amidinophenyl)furan and its prodrug across intestinal epithelium)
IT Human
Lipophilicity
Partition
(mechanisms of transport of **antimicrobial** bis(amidinophenyl)furan and its prodrug across intestinal epithelium)
IT **Drug delivery** systems
(prodrugs; mechanisms of transport of **antimicrobial** bis(amidinophenyl)furan and its prodrug across intestinal epithelium)
IT **73819-26-8**, DB 75 **186953-56-0**, DB289
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of transport of **antimicrobial** bis(amidinophenyl)furan and its prodrug across intestinal epithelium)
IT 14127-61-8, Calcium ion, biological studies
RL: BSU (Biological study, unclassified); MOA (Modifier or additive use); BIOL (Biological study); USES (Uses)
(mechanisms of transport of **antimicrobial** bis(amidinophenyl)furan and its prodrug across intestinal epithelium)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 23 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:555455 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 137:109199
TITLE: Preparation of bis(amidino- and guanidinophenyl)furans and analogs as **microbicides**
INVENTOR(S): Boykin, David; Tidwell, Richard R.; Wilson, W. David; Perfect, John R.; Stephens, Chad E.
PATENT ASSIGNEE(S): University of North Carolina at Chapel Hill,

	USA; Georgia State University Research Foundation, Inc.
SOURCE:	PCT Int. Appl., 36 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057224	A2	20020725	WO 2001-US47238	2001 1106
WO 2002057224	A3	20030306		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002156098	A1	20021024	US 2001-985590	2001 1105
US 6706754	B2	20040316		
CA 2425135	AA	20020725	CA 2001-2425135	2001 1106
US 2003083362	A1	20030501	US 2001-8535	2001 1106
US 6737440	B2	20040518		
EP 1337510	A2	20030827	EP 2001-994174	2001 1106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517889	T2	20040617	JP 2002-557905	2001 1106
US 2004235927	A1	20041125	US 2004-791425	2004 0302

PRIORITY APPLN. INFO.:	US 2000-246244P	P 2000 1106
	US 2000-246330P	P 2000 1107
	US 2001-288428P	P 2001 0504
	US 2001-8535	A3 2001 1106
	WO 2001-US47238	W

2001
1106

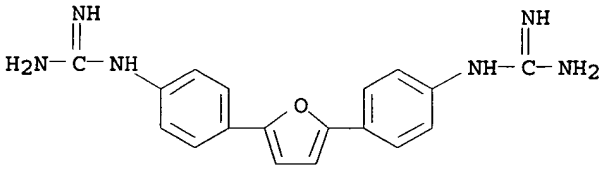
OTHER SOURCE(S): MARPAT 137:109199

AB Z[Z1NHC(:NR5)R6]2 [I; R5 = H, alkyl, aryl; R6 = H, alkyl, aryl, NR7R8; R7,R8 = H, alkyl, aryl; Z = furan-, thiophene-, or pyrrole-2,5-diyl; Z1 = (un)substituted 1,4-phenylene] were prepared Thus, 2,5-bis(tributylstannyl)furan was condensed with 2-bromo-5-nitrotoluene and the product reduced to give 2,5-bis(4-amino-2-methylphenyl)furan. Similarly prepared 2,5-bis(4-aminophenyl)furan was amidated by BzCl and the product converted in 2 steps to I (R5 = H, R6 = Ph, Z = furan-2,5-diyl, Z1 = 1,4-phenylene). Data for biol. activity of I were given.

IT **347190-93-6P 347190-94-7P 347190-95-8P**
347190-96-9P 347190-97-0P 347190-98-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bis(amidino- and guanidinophenyl)furans and analogs as **microbicides**)

RN 347190-93-6 HCAPLUS

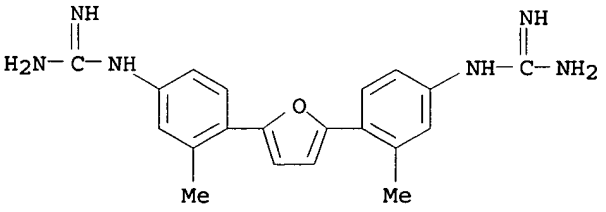
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 347190-94-7 HCAPLUS

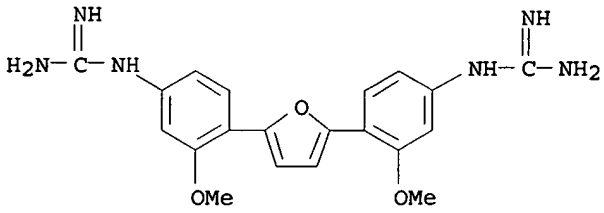
CN Guanidine, N,N'''-[2,5-furandiylbis(3-methyl-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

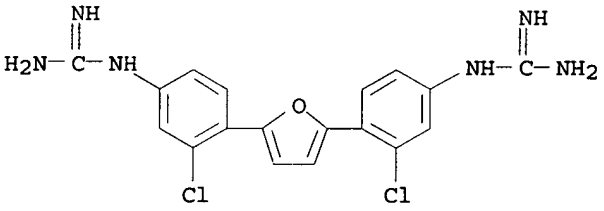
RN 347190-95-8 HCAPLUS

CN Guanidine, N,N'''-[2,5-furandiylbis(3-methoxy-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



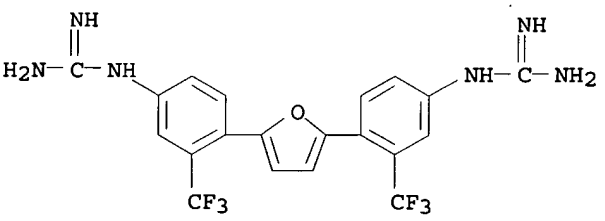
●2 HCl

RN 347190-96-9 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-chloro-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



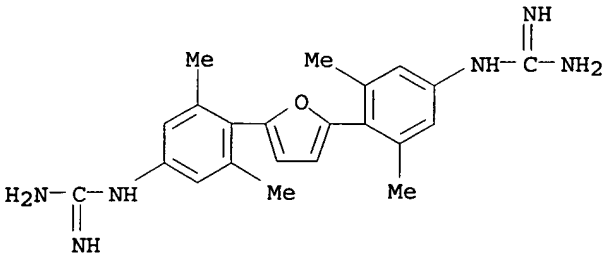
●2 HCl

RN 347190-97-0 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis[3-(trifluoromethyl)-4,1-phenylene]]bis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

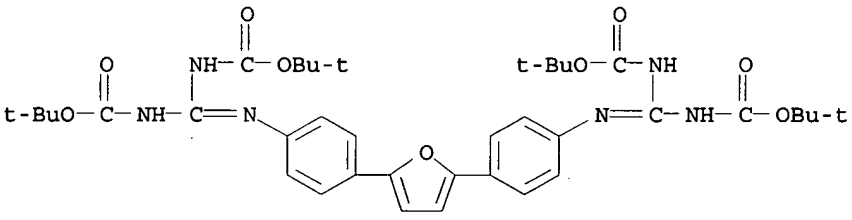
RN 347190-98-1 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3,5-dimethyl-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



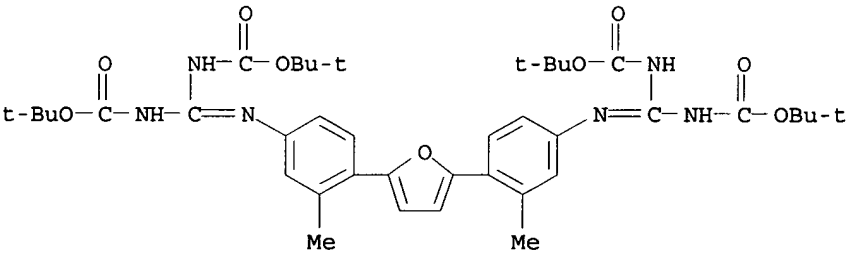
●2 HCl

IT **347190-87-8P 347190-88-9P 347190-89-0P**
347190-90-3P 347190-91-4P 347190-92-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bis(amidino- and guanidinophenyl)furans and analogs as **microbicides**)

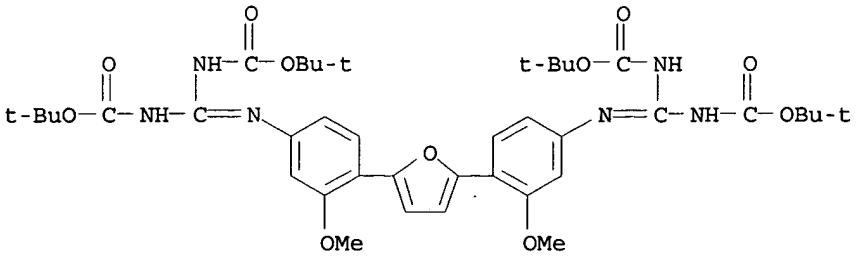
RN 347190-87-8 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenenitrilomethanetetrayl)]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



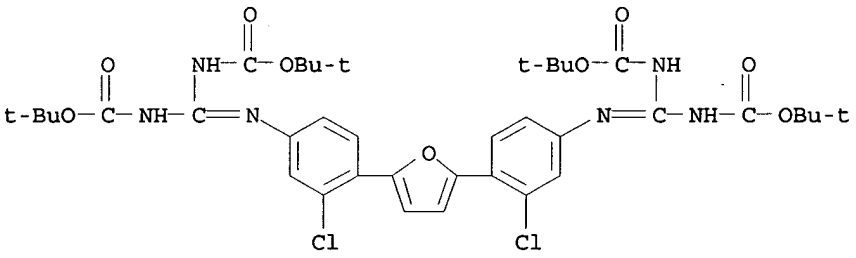
RN 347190-88-9 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3-methyl-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



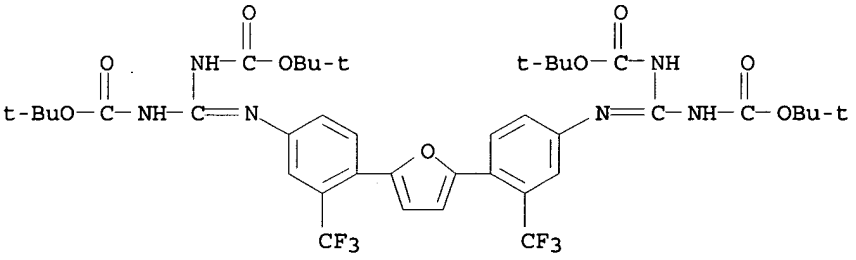
RN 347190-89-0 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3-methoxy-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



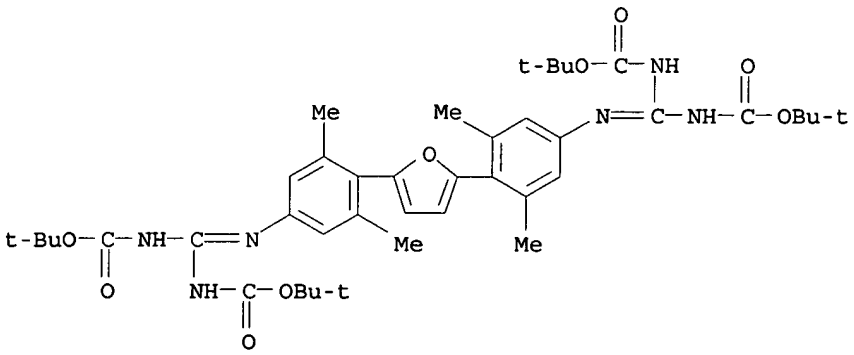
RN 347190-90-3 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3-chloro-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 347190-91-4 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[[3-(trifluoromethyl)-4,1-phenylene]nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 347190-92-5 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3,5-dimethyl-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



IC ICM C07D
CC 27-6 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
ST amidinophenylfuran prepn **microbicide**; bactericide amidinophenylfuran prepn; fungicide amidinophenylfuran prepn; protozoacide amidinophenylfuran prepn
IT Aspergillus
Candida albicans
Cryptococcus neoformans
Cryptosporidium parvum
Fusarium solani
Giardia lamblia
Mycobacterium tuberculosis
Plasmodium (malarial genus)
Pneumocystis carinii
Toxoplasma gondii
Trypanosoma
(infection; treatment; preparation of bis(amidino- and guanidinophenyl)furans and analogs as **microbicides**)
IT Antibacterial agents
Fungicides
Human
Protozoacides
(preparation of bis(amidino- and guanidinophenyl)furans and analogs as **microbicides**)
IT **347190-93-6P 347190-94-7P 347190-95-8P**
347190-96-9P 347190-97-0P 347190-98-1P
347190-99-2P 347191-00-8P 347191-02-0P 347191-03-1P
347191-04-2P 347191-05-3P 347191-06-4P 347191-07-5P
347191-08-6P 347191-09-7P 347191-11-1P 347191-14-4P
347191-15-5P 347191-16-6P 347191-17-7P 347191-18-8P
347191-19-9P 347191-20-2P 347191-21-3P 423165-09-7P
423165-12-2P 423165-54-2P 443797-77-1P 443797-78-2P
443797-79-3P 443797-80-6P 443797-81-7P 443797-83-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bis(amidino- and guanidinophenyl)furans and analogs as **microbicides**)
IT 98-88-4, Benzoyl chloride 100-70-9, 2-Cyanopyridine 874-60-2, 4-Methylbenzoyl chloride 939-26-4, 2-(Bromomethyl)naphthalene 1620-77-5, 2-Cyano-5-methylpyridine 7149-70-4, 2-Bromo-5-nitrotoluene 193361-76-1, 2,5-Bis(tributylstannyl)furan
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of bis(amidino- and guanidinophenyl)furans and analogs as **microbicides**)
IT 5346-38-3P, 2-Thiocarbamoylpyridine 53715-17-6P 56297-30-4P, 2,5-Bis(4-nitrophenyl)furan 251577-90-9P 334017-98-0P

347190-78-7P 347190-79-8P 347190-80-1P 347190-81-2P
347190-82-3P 347190-83-4P 347190-84-5P 347190-85-6P
347190-86-7P **347190-87-8P 347190-88-9P**
347190-89-0P 347190-90-3P 347190-91-4P
347190-92-5P 347191-01-9P 347191-10-0P 347191-22-4P
347191-23-5P 347191-24-6P 347191-25-7P 443797-82-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bis(amidino- and guanidinophenyl)furans and analogs as **microbicides**)

L42 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:539483 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 137:103864
TITLE: Compounds useful for the treatment of bovine viral diarrhea virus and hepatitis C virus infections
INVENTOR(S): Boykin, David; Tidwell, Richard R.; Stringfellow, David; Brock, Kenny; Stephens, Chad E.; Kumar, Arvind; Wilson, W. David; Givens, Daniel; Dykstra, Christine
PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA; Georgia State University Research Foundation; Auburn University
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055025	A2	20020718	WO 2002-US787	2002 0111
WO 2002055025	A3	20040115		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2433070	AA	20020718	CA 2002-2433070	2002 0111
US 2003199521	A1	20031023	US 2002-44315	2002 0111
EP 1399163	A2	20040324	EP 2002-705743	2002 0111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004525881	T2	20040826	JP 2002-555762	2002 0111
PRIORITY APPLN. INFO.:			US 2001-261654P P	2001 0113

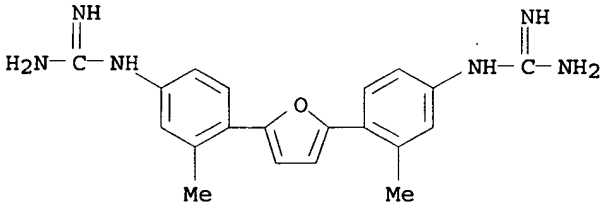
WO 2002-US787 W
2002
0111

OTHER SOURCE(S): MARPAT 137:103864

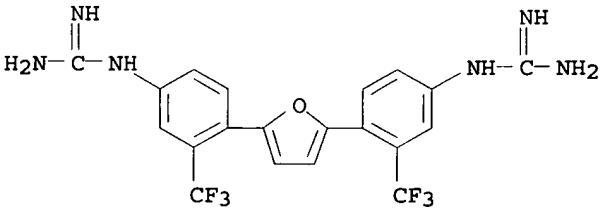
AB The invention relates to novel compds. and methods that are useful in treating members of the Flaviviridae family of viruses. Compds. disclosed in the invention are shown to be effective against bovine viral diarrhea virus and hepatitis C virus infection.

IT **423165-10-0 423165-11-1 423165-30-4 423165-31-5 442842-44-6 442842-45-7 442842-48-0 442842-49-1 442842-50-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. for treatment of bovine viral diarrhea virus infection and hepatitis C virus infection)

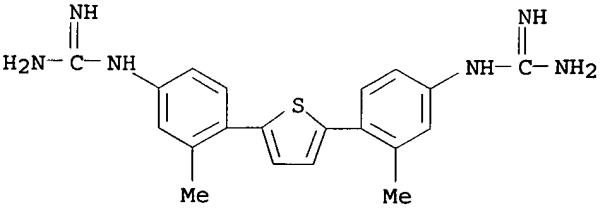
RN 423165-10-0 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-methyl-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



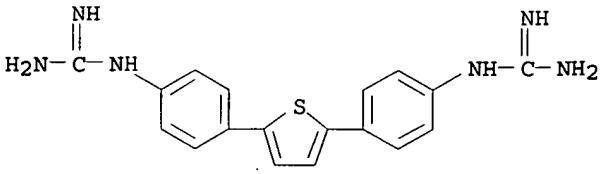
RN 423165-11-1 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis[3-(trifluoromethyl)-4,1-phenylene]]bis- (9CI) (CA INDEX NAME)



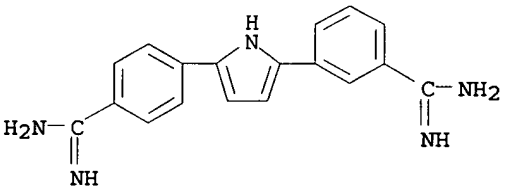
RN 423165-30-4 HCAPLUS
CN Guanidine, N,N'''-[2,5-thiophenediylbis(3-methyl-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



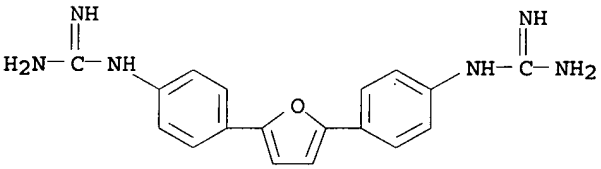
RN 423165-31-5 HCAPLUS
CN Guanidine, N,N'''-(2,5-thiophenediyldi-4,1-phenylene)bis- (9CI) (CA INDEX NAME)



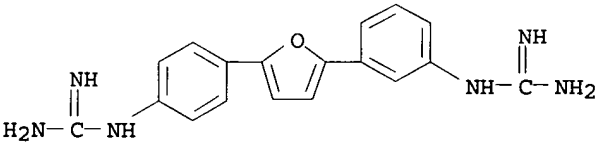
RN 442842-44-6 HCAPLUS
CN Benzenecarboximidamide, 3-[5-[4-(aminoiminomethyl)phenyl]-1H-pyrrol-2-yl]- (9CI) (CA INDEX NAME)



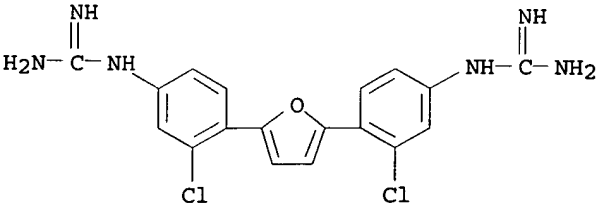
RN 442842-45-7 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis- (9CI) (CA INDEX NAME)



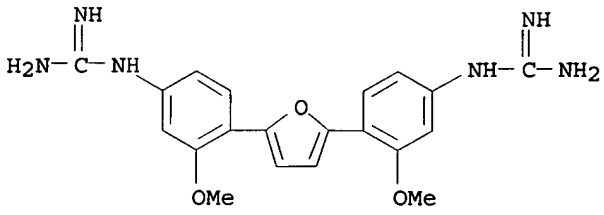
RN 442842-48-0 HCAPLUS
CN Guanidine, [3-[5-[4-[(aminoiminomethyl)amino]phenyl]-2-furanyl]phenyl]- (9CI) (CA INDEX NAME)



RN 442842-49-1 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-chloro-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)

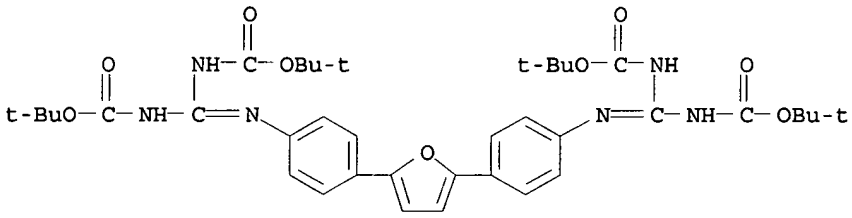


RN 442842-50-4 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-methoxy-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)

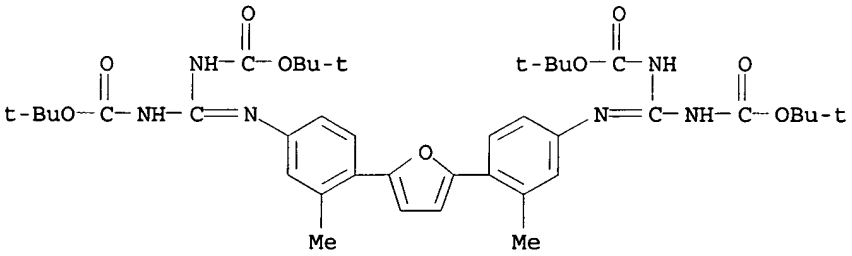


IT **347190-87-8P 347190-88-9P 347190-89-0P**
347190-90-3P 347190-91-4P 347190-92-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(compds. for treatment of bovine viral diarrhea virus infection and hepatitis C virus infection)

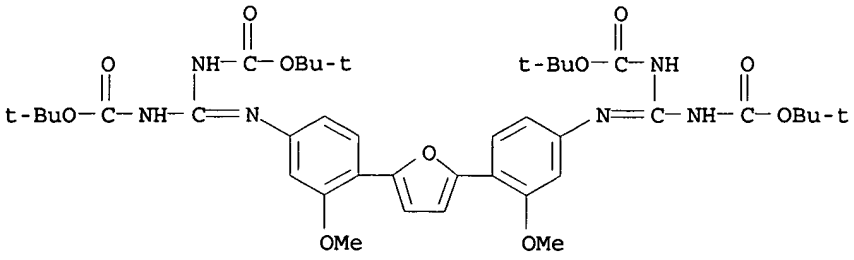
RN 347190-87-8 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenenitrilomethanetetrayl)]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



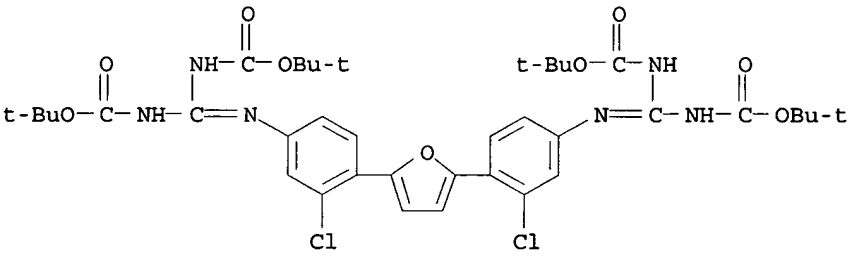
RN 347190-88-9 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3-methyl-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



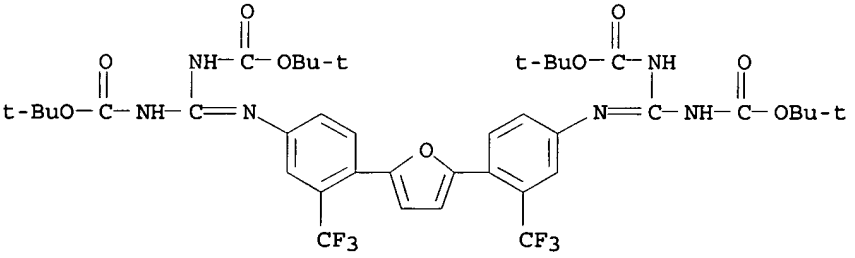
RN 347190-89-0 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3-methoxy-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



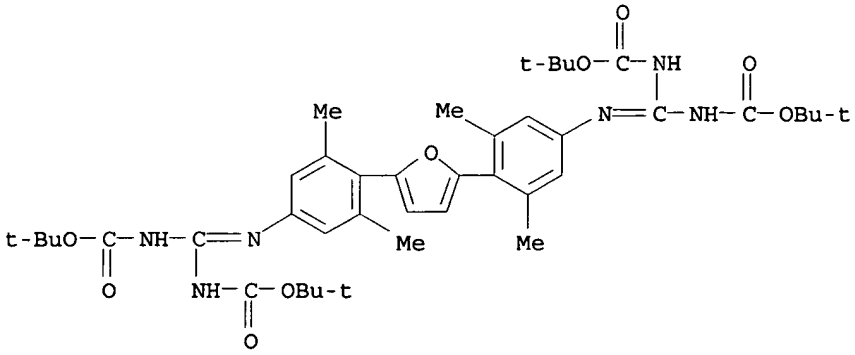
RN 347190-90-3 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3-chloro-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 347190-91-4 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[[3-(trifluoromethyl)-4,1-phenylene]nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

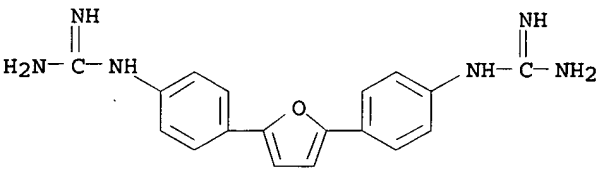


RN 347190-92-5 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3,5-dimethyl-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



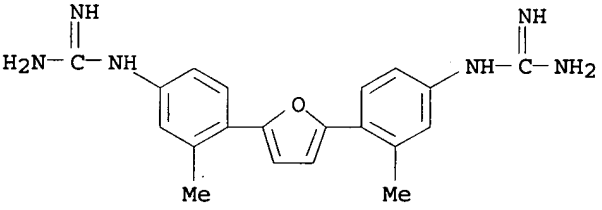
IT **347190-93-6P 347190-94-7P 347190-95-8P**
347190-96-9P 347190-97-0P 347190-98-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(compds. for treatment of bovine viral diarrhea virus infection and hepatitis C virus infection)

RN 347190-93-6 HCAPLUS
CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis-, dihydrochloride (9CI) (CA INDEX NAME)



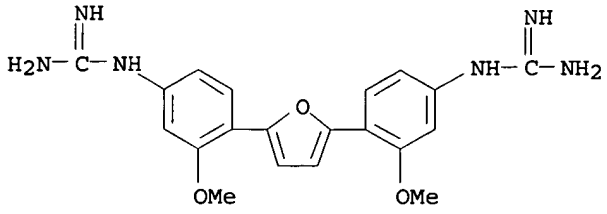
●2 HCl

RN 347190-94-7 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-methyl-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



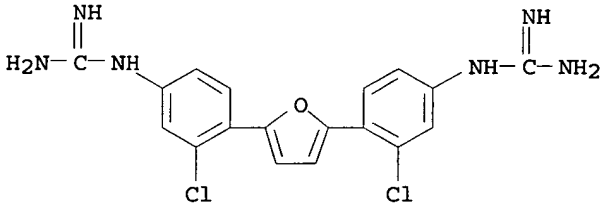
●2 HCl

RN 347190-95-8 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-methoxy-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



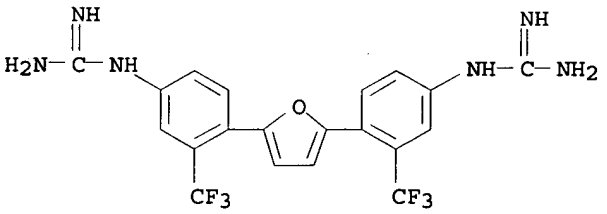
●2 HCl

RN 347190-96-9 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-chloro-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



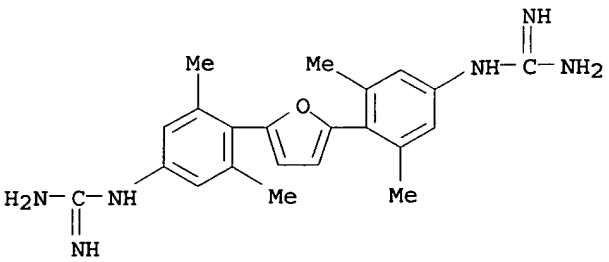
●2 HCl

RN 347190-97-0 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis[3-(trifluoromethyl)-4,1-phenylene]]bis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 347190-98-1 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3,5-dimethyl-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

IC ICM A61K
CC 1-5 (Pharmacology)
Section cross-reference(s): 28
IT **Drug delivery** systems
(injections, i.v.; compds. for treatment of bovine viral diarrhea virus infection and hepatitis C virus infection)
IT **Drug delivery** systems
(oral; compds. for treatment of bovine viral diarrhea virus infection and hepatitis C virus infection)
IT **423165-10-0 423165-11-1 423165-30-4**
423165-31-5 433735-86-5 433735-89-8 433735-90-1
442842-40-2 442842-41-3 442842-42-4 442842-43-5
442842-44-6 442842-45-7 442842-46-8
442842-47-9 **442842-48-0 442842-49-1**
442842-50-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. for treatment of bovine viral diarrhea virus infection and hepatitis C virus infection)
IT 53715-17-6P 56297-30-4P 251577-90-9P 332360-11-9P
347190-78-7P 347190-79-8P 347190-80-1P 347190-81-2P
347190-82-3P 347190-83-4P 347190-84-5P 347190-85-6P
347190-86-7P **347190-87-8P 347190-88-9P**
347190-89-0P 347190-90-3P 347190-91-4P
347190-92-5P 442842-52-6P 442842-54-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(compds. for treatment of bovine viral diarrhea virus infection and hepatitis C virus infection)
IT **347190-93-6P 347190-94-7P 347190-95-8P**
347190-96-9P 347190-97-0P 347190-98-1P
442842-51-5P 442842-53-7P 442842-55-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(compds. for treatment of bovine viral diarrhea virus infection and hepatitis C virus infection)

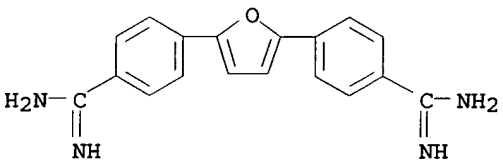
L42 ANSWER 25 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:431606 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 137:379622
TITLE: Characterizing the fragmentation of 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime and selected metabolites using ion trap mass spectrometry
AUTHOR(S): Zhou, Lian; Voyksner, Robert D.; Thakker, Dhiren R.; Stephens, Chad E.; Anbazhagan, Mariappan; Boykin, David W.; Hall, James E.; Tidwell, Richard R.
CORPORATE SOURCE: Division of Medicinal Chemistry and Natural Products, School of Pharmacy, The University

of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA
SOURCE: Rapid Communications in Mass Spectrometry (2002), 16(11), 1078-1085
CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

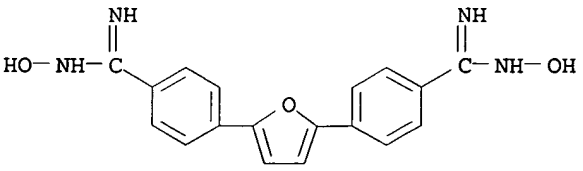
AB A novel prodrug [2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime (DB289)] of the promising **antimicrobial** agent, 2,5-bis(4-amidinophenyl)furan (DB75), has excellent oral activity. It is currently undergoing phase II clin. evaluation as an orally administered drug candidate against African trypanosomiasis and Pneumocystis carinii pneumonia. The sequential product ion (MSn) fragmentations of DB289 and selected metabolites were characterized using ion trap mass spectrometry with electrospray ionization. An unusual homolytic bond cleavage, formation of an odd-electron ion from an even-electron ion with the loss of a radical, was commonly seen in the fragmentation patterns of DB289 and its metabolites. Both O-Et and N-Me homologs of DB289 were utilized to confirm this fragmentation pathway. The labile hydrogen atoms in DB289 are readily exchanged with deuterium atoms in the solvent containing deuterium oxide (D2O) instead of water. The mass shift patterns displayed in the product ion spectra of DB289 in D2O proved useful in verifying the fragmentation pathway. Octadeuterated DB289 and DB75 (d-labeling on the di-Ph rings) showed unequivocally that the diphenylfuran moiety is not involved in the fragmentation. The fragmentation pathways uncovered in this work will facilitate structural characterization of all the metabolites produced in the metabolic activation of DB289.

IT **73819-26-8**, DB 75 **186953-55-9**
186953-56-0, DB 289 **186953-57-1**
336786-81-3 336786-82-4 475976-07-9
475976-08-0
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(characterizing the fragmentation of 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime and selected metabolites using ion trap mass spectrometry)

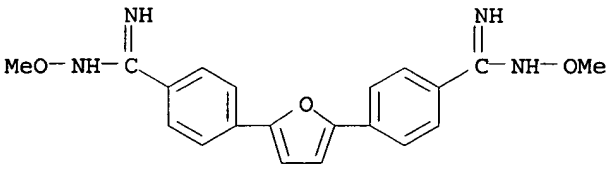
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



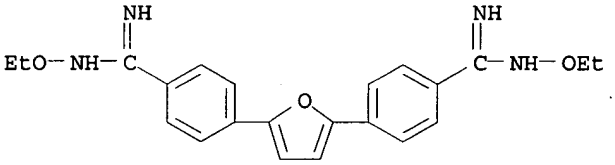
RN 186953-55-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



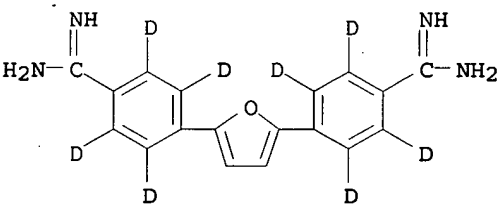
RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



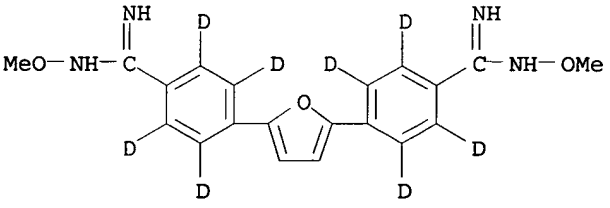
RN 186953-57-1 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-ethoxy- (9CI) (CA INDEX NAME)



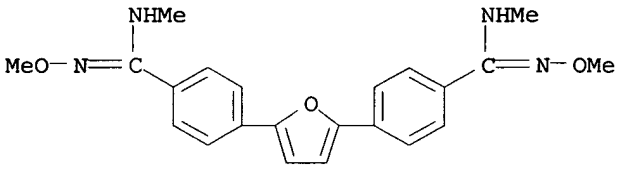
RN 336786-81-3 HCAPLUS
CN Benzene-2,3,5,6-d4-carboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



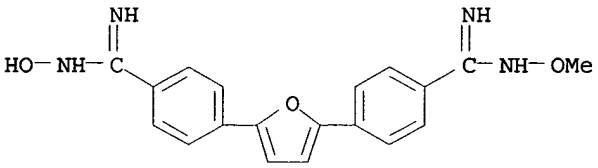
RN 336786-82-4 HCAPLUS
CN Benzene-2,3,5,6-d4-carboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



RN 475976-07-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy-N'-methyl- (9CI) (CA INDEX NAME)



RN 475976-08-0 HCAPLUS
CN Benzenecarboximidamide, 4-[5-[4-[(hydroxyamino)iminomethyl]phenyl]-2-furanyl]-N-methoxy- (9CI) (CA INDEX NAME)



CC 1-1 (Pharmacology)
IT **73819-26-8**, DB 75 **186953-55-9**
186953-56-0, DB 289 **186953-57-1**
336786-81-3 336786-82-4 475976-07-9
475976-08-0
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(characterizing the fragmentation of 2,5-bis(4-amidinophenyl)furan-bis-O-methylamidoxime and selected metabolites using ion trap mass spectrometry)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:353451 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 136:363813
TITLE: Reversed amidines and methods of using them for treating, preventing, or inhibiting leishmaniasis
INVENTOR(S): Werbovetz, Karl A.; Brendle, James J.; Boykin, David W.; Stephens, Chad E.
PATENT ASSIGNEE(S): U.S. Army Medical Research and Material Command, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036588	A2	20020510	WO 2001-US42905	2001 1105
WO 2002036588	A3	20030828		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,

MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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US 2002156098	A1	20021024	US 2001-985590	2001 1105
US 6706754	B2	20040316		
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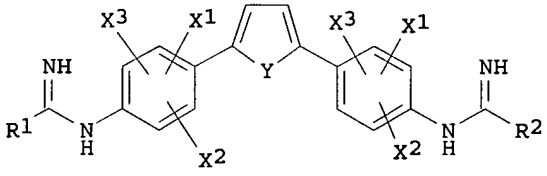
			US 2000-246244P	P 2000 1106
			WO 2001-US42905	W 2001 1105

OTHER SOURCE(S): MARPAT 136:363813
GI



I

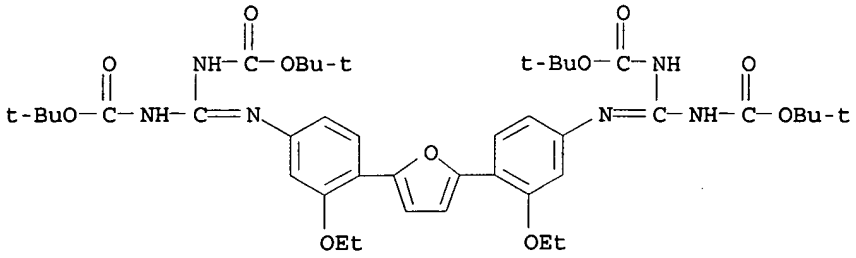
AB Methods are disclosed for treating, preventing or inhibiting leishmaniasis in a subject which comprise administering to the subject a therapeutically effective amount of at least one compound I (Y = heteroatom; R1, R2 = H, alkyl, cycloalkyl, heterocycloalkyl, aryl, amino, heteroaryl; X1, X2, X3 = H, alkyl, alkoxy, halo, amino, alkylamino, dialkylamino, acylamino, alkylthio, sulfonyl, cyano, carboxy, alkoxycarbonyl, carbamoyl).

IT **423165-60-0P 423165-63-3P 423165-65-5P 423165-67-7P 423165-70-2P 423165-73-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; reversed amidines for treating, preventing, or inhibiting leishmaniasis)

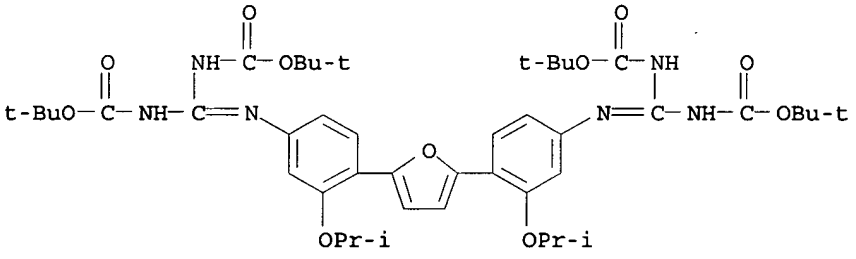
RN 423165-60-0 HCAPLUS

CN Carbamic acid, [2,5-furandiylbis[(3-ethoxy-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-

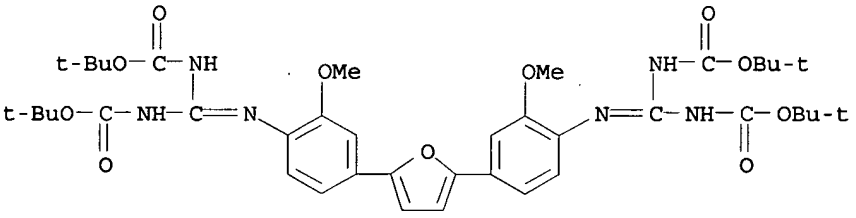
dimethylethyl) ester (9CI) (CA INDEX NAME)



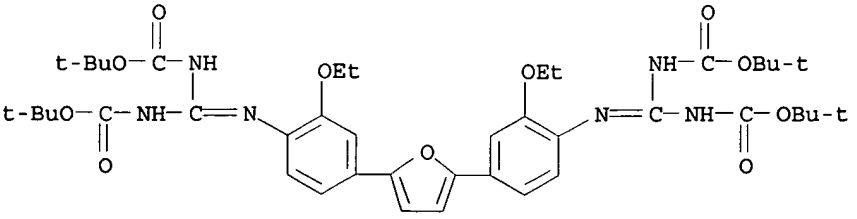
RN 423165-63-3 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[[3-(1-methylethoxy)-4,1-phenylene]nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 423165-65-5 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(2-methoxy-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

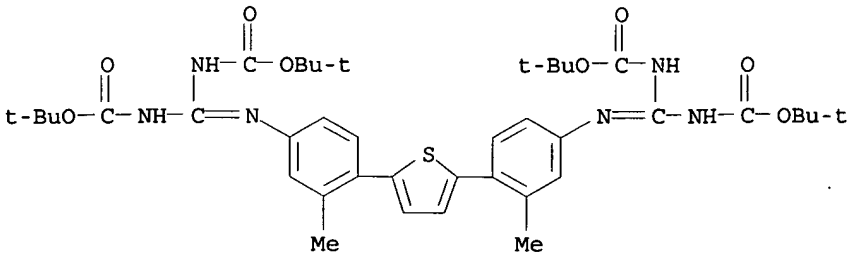


RN 423165-67-7 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(2-ethoxy-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

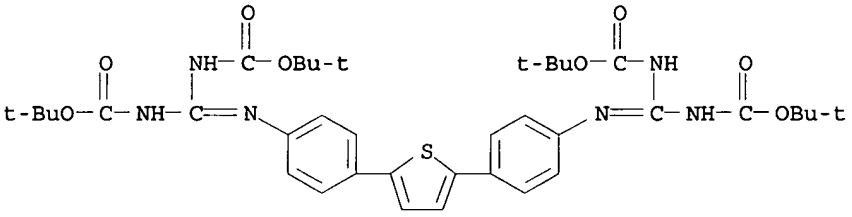


RN 423165-70-2 HCAPLUS

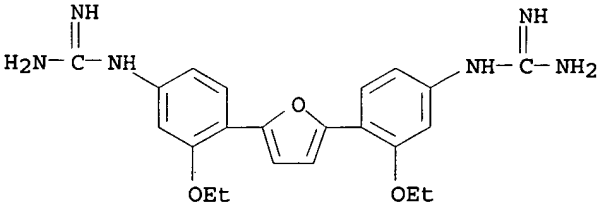
CN Carbamic acid, [2,5-thiophenediylbis[(3-methyl-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



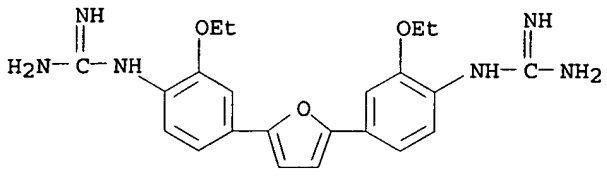
RN 423165-73-5 HCAPLUS
CN Carbamic acid, [2,5-thiophenediylbis(4,1-phenylenenitrilomethanetetrayl)]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



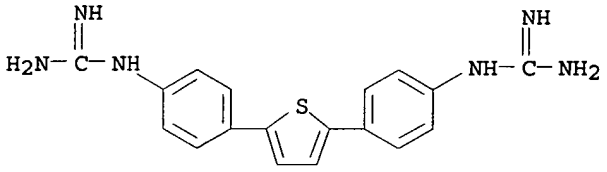
IT **423165-25-7P 423165-28-0P 423165-31-5P 423165-62-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reversed amidines for treating, preventing, or inhibiting leishmaniasis)
RN 423165-25-7 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-ethoxy-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



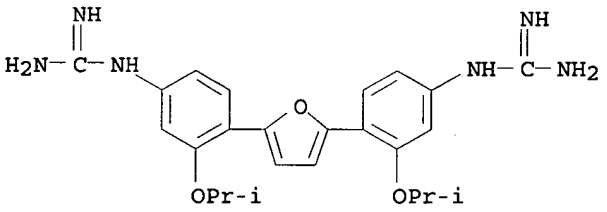
RN 423165-28-0 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(2-ethoxy-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



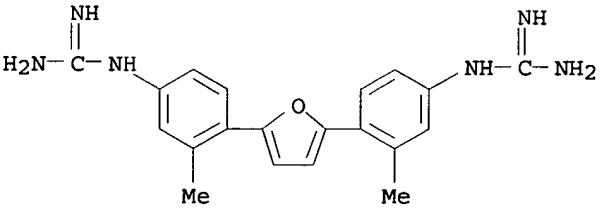
RN 423165-31-5 HCAPLUS
CN Guanidine, N,N'''-(2,5-thiophenediyldi-4,1-phenylene)bis- (9CI) (CA INDEX NAME)



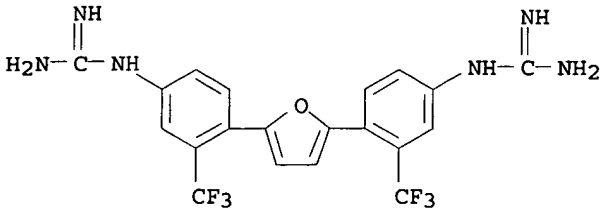
RN 423165-62-2 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis[3-(1-methylethoxy)-4,1-phenylene]]bis- (9CI) (CA INDEX NAME)



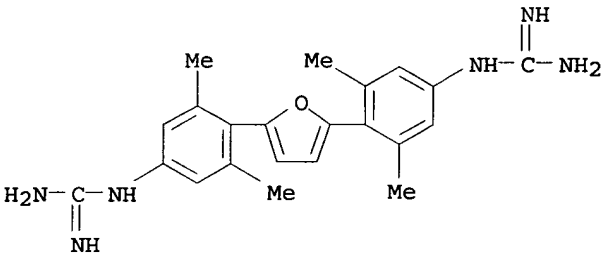
IT **423165-10-0 423165-11-1 423165-16-6 423165-19-9 423165-26-8 423165-27-9 423165-30-4 423165-75-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reversed amidines for treating, preventing, or inhibiting leishmaniasis)
RN 423165-10-0 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-methyl-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



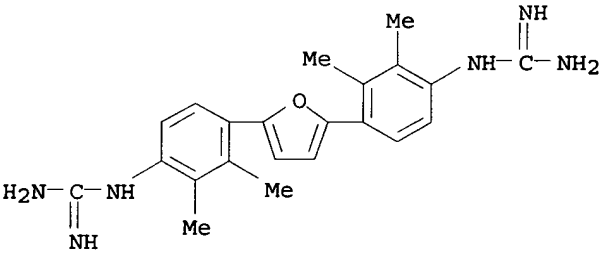
RN 423165-11-1 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis[3-(trifluoromethyl)-4,1-phenylene]]bis- (9CI) (CA INDEX NAME)



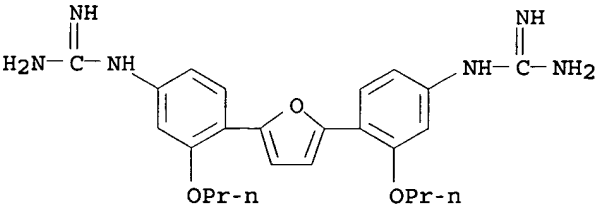
RN 423165-16-6 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3,5-dimethyl-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



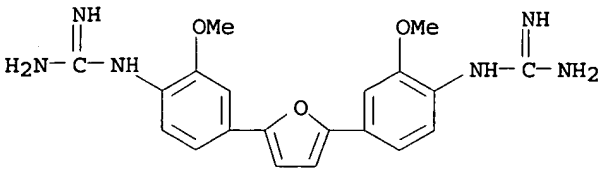
RN 423165-19-9 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(2,3-dimethyl-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



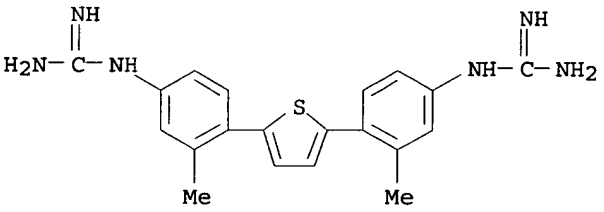
RN 423165-26-8 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-propoxy-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



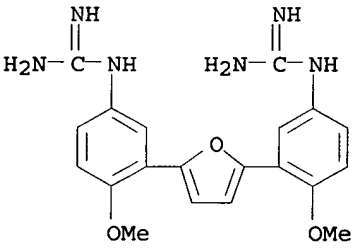
RN 423165-27-9 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(2-methoxy-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



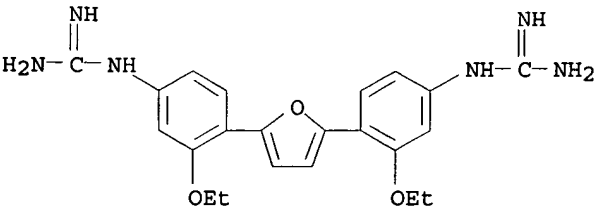
RN 423165-30-4 HCAPLUS
CN Guanidine, N,N'''-[2,5-thiophenediylbis(3-methyl-4,1-phenylene)]bis- (9CI) (CA INDEX NAME)



RN 423165-75-7 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(4-methoxy-3,1-phenylene)]bis- (9CI) (CA INDEX NAME)

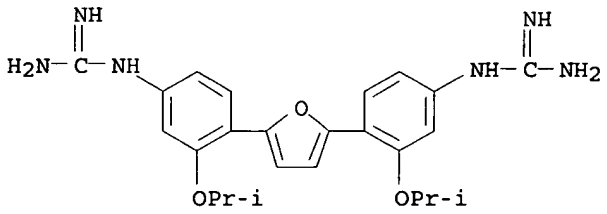


IT **423165-61-1P 423165-64-4P 423165-66-6P**
423165-69-9P 423165-71-3P 423165-74-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(reversed amidines for treating, preventing, or inhibiting leishmaniasis)
RN 423165-61-1 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-ethoxy-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



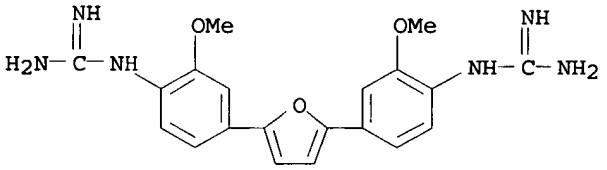
●2 HCl

RN 423165-64-4 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis[3-(1-methylethoxy)-4,1-phenylene]]bis-, dihydrochloride (9CI) (CA INDEX NAME)



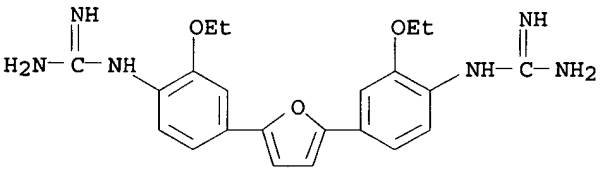
●2 HCl

RN 423165-66-6 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(2-methoxy-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



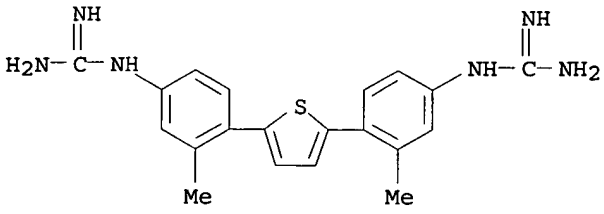
●2 HCl

RN 423165-69-9 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(2-ethoxy-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



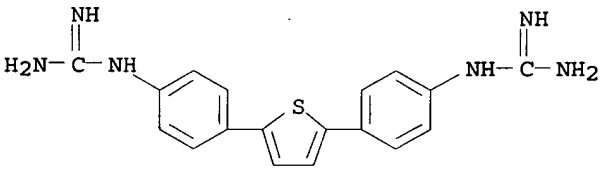
●2 HCl

RN 423165-71-3 HCAPLUS
CN Guanidine, N,N'''-[2,5-thiophenediylbis(3-methyl-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 423165-74-6 HCAPLUS
CN Guanidine, N,N'''-(2,5-thiophenediyldi-4,1-phenylene)bis-, dihydrochloride (9CI) (CA INDEX NAME)



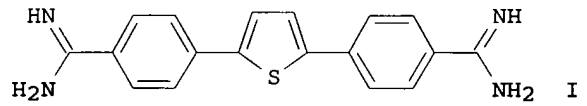
●2 HCl

IC ICM C07D405-00
CC 1-5 (Pharmacology)
IT **Drug delivery** systems
Leishmania
Leishmania donovani
Leishmania mexicana
Parasiticides
(reversed amidines for treating, preventing, or inhibiting leishmaniasis)
IT 7035-69-0P 53715-17-6P 56297-30-4P 57279-70-6P
101793-47-9P 103966-66-1P 251577-90-9P 347190-78-7P
347190-79-8P 347190-80-1P 347190-81-2P 347190-82-3P
347190-83-4P 347190-84-5P 347190-86-7P 423165-32-6P
423165-34-8P 423165-35-9P 423165-36-0P 423165-37-1P
423165-39-3P 423165-42-8P 423165-48-4P 423165-49-5P
423165-50-8P 423165-51-9P 423165-52-0P **423165-60-0P**
423165-63-3P 423165-65-5P 423165-67-7P
423165-70-2P 423165-73-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; reversed amidines for treating, preventing, or inhibiting leishmaniasis)
IT 347190-99-2P 347191-03-1P 347191-04-2P 347191-07-5P
347191-09-7P 347191-14-4P 347191-16-6P 347191-18-8P
347191-20-2P 423165-06-4P 423165-09-7P 423165-22-4P
423165-25-7P 423165-28-0P 423165-29-1P
423165-31-5P 423165-62-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reversed amidines for treating, preventing, or inhibiting leishmaniasis)
IT **423165-10-0 423165-11-1** 423165-12-2

423165-14-4 423165-15-5 **423165-16-6** 423165-17-7
423165-18-8 **423165-19-9** 423165-20-2 423165-21-3
423165-23-5 423165-24-6 **423165-26-8**
423165-27-9 423165-30-4 423165-75-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reversed amidines for treating, preventing, or inhibiting leishmaniasis)

IT 347190-85-6P 347191-00-8P 347191-05-3P 347191-08-6P
347191-11-1P 347191-15-5P 347191-17-7P 347191-19-9P
347191-21-3P 423165-54-2P 423165-55-3P 423165-56-4P
423165-57-5P 423165-58-6P 423165-59-7P **423165-61-1P**
423165-64-4P 423165-66-6P 423165-69-9P
423165-71-3P 423165-74-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(reversed amidines for treating, preventing, or inhibiting leishmaniasis)

L42 ANSWER 27 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:146280 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 136:321920
TITLE: Antileishmanial activities of several classes of aromatic dications
AUTHOR(S): Brendle, James J.; Outlaw, Abram; Kumar, Arvind; Boykin, David W.; Patrick, Donald A.; Tidwell, Richard R.; Werbovetz, Karl A.
CORPORATE SOURCE: Division of Experimental Therapeutics, Walter Reed Army Institute of Research, Silver Spring, MD, 20910, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2002), 46(3), 797-807
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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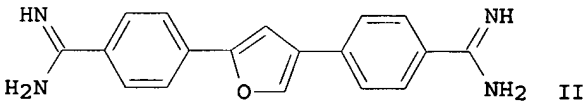


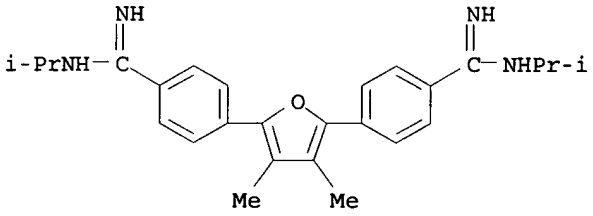
II

AB Aromatic dicationic mols. possess impressive activity against a broad spectrum of **microbial** pathogens, including Pneumocystis carinii, Cryptosporidium parvum, and Candida albicans. In this work, 58 aromatic cations were examined for inhibitory activity against axenic amastigote-like Leishmania donovani parasites. In general, the most potent of the compds. were substituted di-Ph furan and thiophene dications. 2,5-Bis-(4-amidinophenyl)thiophene (I) was the most active compound This agent displayed a 50% inhibitory concentration (IC50) of 0.42 ± 0.08 μM against L. donovani and an in vitro antileishmanial potency 6.2-fold greater than that of the clin. antileishmanial dication pentamidine and was 155-fold more toxic to the parasites than to a mouse macrophage cell line. 2,4-Bis-(4-amidinophenyl)furan (II) was twice as active as pentamidine (IC50, 1.30 ± 0.21 μM), while 2,5-bis-(4-amidinophenyl)furan and pentamidine were essentially equipotent in our in vitro antileishmanial assay. Carbazoles,

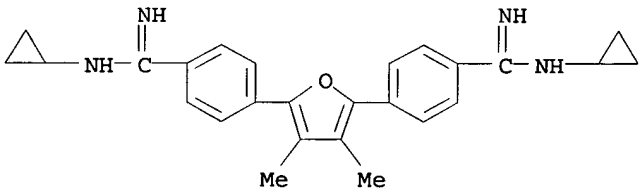
dibenzofurans, dibenzothiophenes, and benzimidazoles containing amidine or substituted amidine groups were generally less active than the di-Ph furans and thiophenes. In all cases, aromatic dications possessing strong antileishmanial activity were several-fold more toxic to the parasites than to a cultured mouse macrophage cell line. These structure-activity relationships demonstrate the potent antileishmanial activity of several aromatic dications and provide valuable information for the future design and synthesis of more potent antiparasitic agents.

IT **299162-32-6P 415717-81-6P 415717-83-8P 415717-90-7P 415717-91-8P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antileishmanial activities of several classes of aromatic dications)

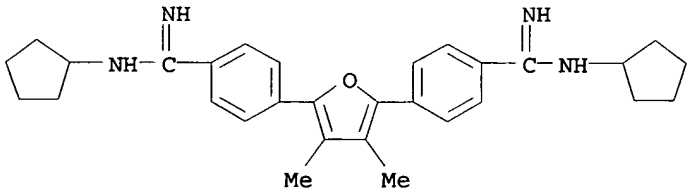
RN 299162-32-6 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3,4-dimethyl-2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



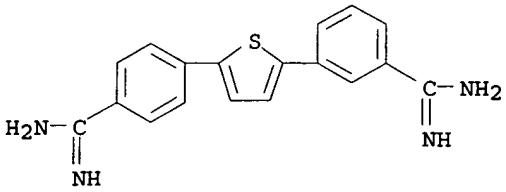
RN 415717-81-6 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3,4-dimethyl-2,5-furandiyl)bis[N-cyclopropyl- (9CI) (CA INDEX NAME)



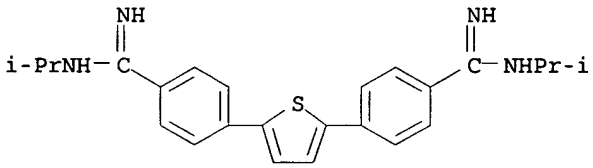
RN 415717-83-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3,4-dimethyl-2,5-furandiyl)bis[N-cyclopentyl- (9CI) (CA INDEX NAME)



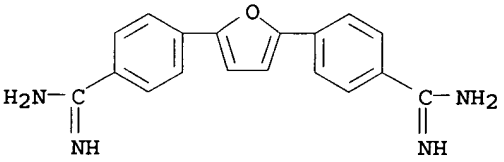
RN 415717-90-7 HCAPLUS
CN Benzenecarboximidamide, 3-[5-[4-(aminoiminomethyl)phenyl]-2-thienyl]- (9CI) (CA INDEX NAME)



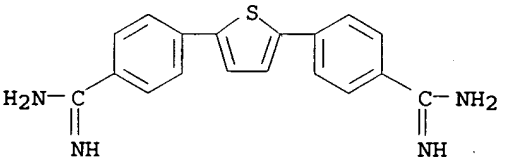
RN 415717-91-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-thiophenediyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



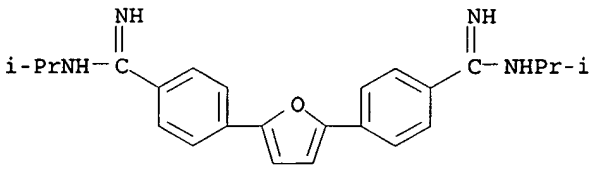
IT **73819-26-8 73819-28-0 173420-56-9**
179118-06-0 179118-22-0 186953-55-9
186953-56-0 192525-51-2 205122-83-4
415717-75-8 415717-76-9 415717-78-1
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antileishmanial activities of several classes of aromatic dications)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



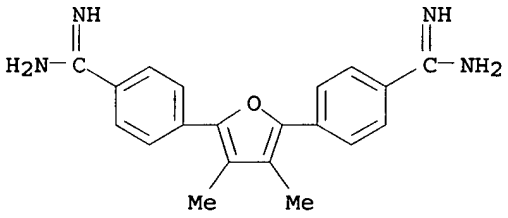
RN 73819-28-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-thiophenediyl)bis- (9CI) (CA INDEX NAME)



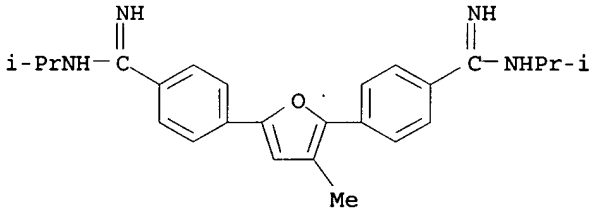
RN 173420-56-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



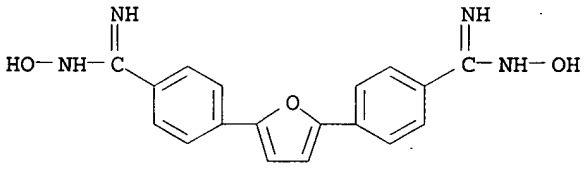
RN 179118-06-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3,4-dimethyl-2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



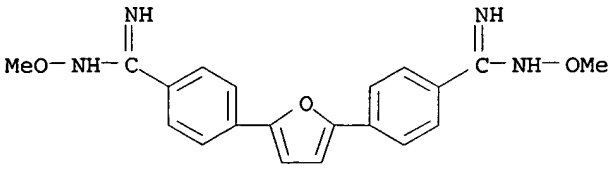
RN 179118-22-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3-methyl-2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



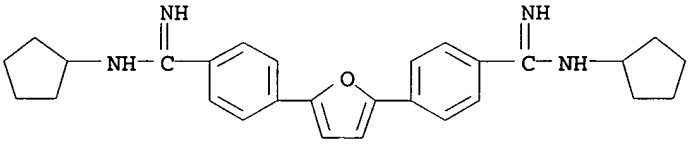
RN 186953-55-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



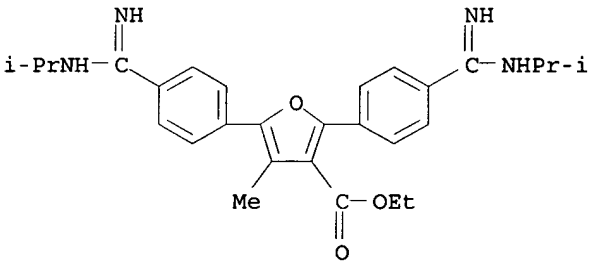
RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



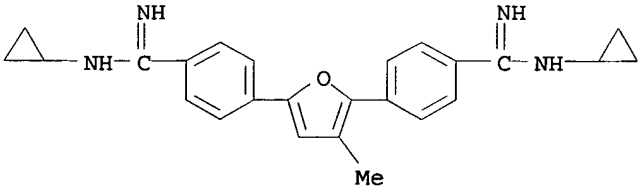
RN 192525-51-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-cyclopentyl- (9CI) (CA INDEX NAME)



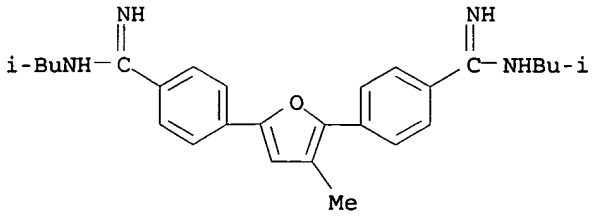
RN 205122-83-4 HCAPLUS
CN 3-Furancarboxylic acid, 2,5-bis[4-[imino[(1-methylethyl)amino]methyl]phenyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)



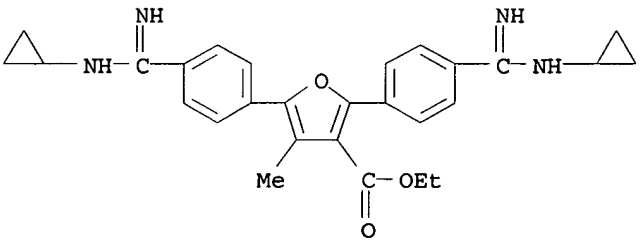
RN 415717-75-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3-methyl-2,5-furandiyl)bis[N-cyclopropyl- (9CI) (CA INDEX NAME)



RN 415717-76-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3-methyl-2,5-furandiyl)bis[N-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 415717-78-1 HCAPLUS
CN 3-Furancarboxylic acid, 2,5-bis[4-[(cyclopropylamino)iminomethyl]phenyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)



CC 10-5 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 1
IT 80498-77-7P **299162-32-6P** 302793-60-8P,
9H-Carbazole-2,6-dicarboximidamide **415717-81-6P**
415717-83-8P 415717-90-7P 415717-91-8P
415717-92-9P 415718-08-0P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antileishmanial activities of several classes of aromatic dications)
IT **73819-26-8 73819-28-0** 80498-71-1
173420-56-9 179118-06-0 179118-22-0
186395-18-6 186395-20-0 186395-22-2 **186953-55-9**
186953-56-0 192525-51-2 200205-81-8
200878-32-6, 9H-Carbazole-3,6-dicarboximidamide 200878-34-8
200878-40-6, 9H-Carbazole-2,7-dicarboximidamide 200878-41-7
200878-43-9 200878-44-0 **205122-83-4** 216502-98-6
216503-06-9 242807-42-7 242807-48-3 242807-54-1
242807-58-5 242807-59-6 338945-24-7, 2,8-Dibenzofurandicarboximidamide **415717-75-8**
415717-76-9 415717-78-1 415717-96-3
415718-04-6 415718-06-8 415718-14-8 415718-17-1
415718-20-6 415718-23-9, 3,7-Dibenzofurandicarboximidamide
415718-26-2 415718-29-5 415718-32-0, 2,8-Dibenzothiophenedicarboximidamide 415718-35-3 415718-38-6
415718-41-1, 3,7-Dibenzothiophenedicarboximidamide 415718-44-4
415718-47-7 415718-50-2 415718-56-8 415718-58-0
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antileishmanial activities of several classes of aromatic dications)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:301099 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 135:76736

TITLE: Diguanidino and "Reversed" Diamidino 2,5-Diarylfurans as **Antimicrobial** Agents

AUTHOR(S): Stephens, Chad E.; Tanious, Farial; Kim, Susan; Wilson, W. David; Schell, Wiley A.; Perfect, John R.; Franzblau, Scott G.; Boykin, David W.

CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303-3083, USA

SOURCE: Journal of Medicinal Chemistry (2001), 44(11), 1741-1748
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:76736

GI

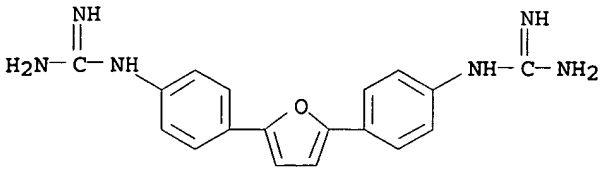
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Dicationic 2,5-bis(4-guanidinophenyl)furans, e.g. I, 2,5-bis[4-(arylimino)aminophenyl]furans, e.g. II, and 2,5-bis[4-(alkylimino)aminophenyl]furans, e.g. III have been synthesized starting from 2,5-bis[tri-n-butylstannyl]furan. Thermal melting studies with poly dA•dT and the duplex oligomer d(CGCGAATTCGCG)2 demonstrated high DNA binding affinities for a number of the compds. The binding affinities are highly dependent on structure and are significantly affected by substituents both on the Ph rings of the 2,5-diphenylfuran nucleus and on the cationic centers. Of the 17 novel dicationic compds. synthesized, six exhibited MICs of 2 μg/mL or less vs. Mycobacterium tuberculosis. Of the compds. screened against Candida albicans, three gave MICs of 2 μg/mL or less (I, II and IV) and two (I, II) were fungicidal, unlike a standard antifungal drug fluconazole, which was fungistatic. In addition, one of the tested compds. II exhibited a MIC of <1 μg/mL against Aspergillus fumigatus, while also being a fungicidal against this organism. Finally, when evaluated against an expanded fungal panel, compound IV showed good activity against Cryptococcus neoformans and Rhizopus arrhizus.

IT **347190-93-6P 347190-94-7P 347190-95-8P 347190-96-9P 347190-97-0P 347190-98-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of bis(guanidinoaryl)- and bis(amidinoaryl)furans as antifungal and antituberculosis agents)

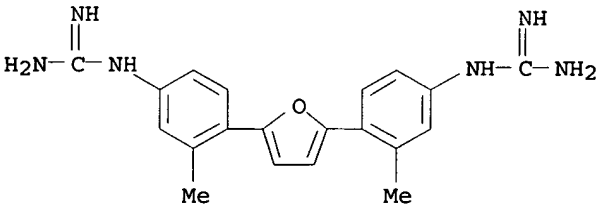
RN 347190-93-6 HCAPLUS

CN Guanidine, N,N'''-(2,5-furandiyldi-4,1-phenylene)bis-, dihydrochloride (9CI) (CA INDEX NAME)



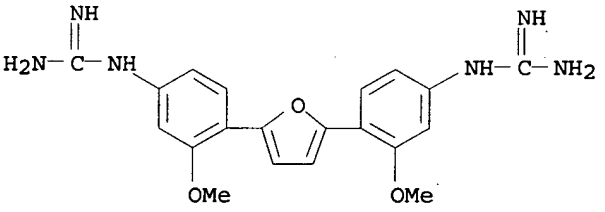
●2 HCl

RN 347190-94-7 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-methyl-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



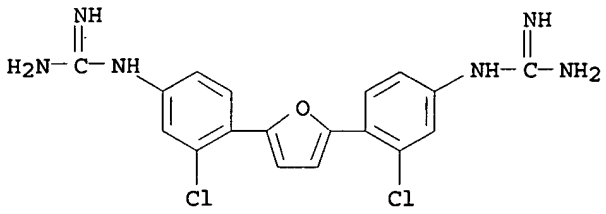
●2 HCl

RN 347190-95-8 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-methoxy-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



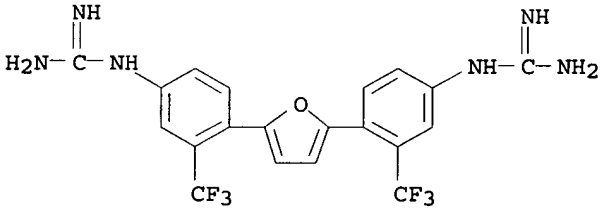
●2 HCl

RN 347190-96-9 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3-chloro-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)



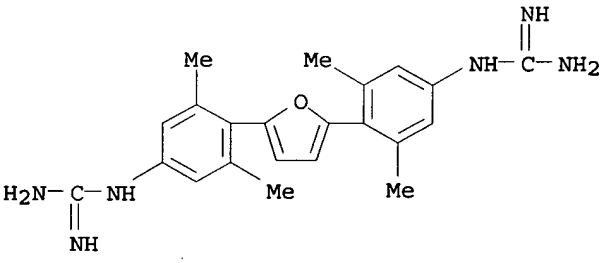
●2 HCl

RN 347190-97-0 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis[3-(trifluoromethyl)-4,1-phenylene]]bis-, dihydrochloride (9CI) (CA INDEX NAME)



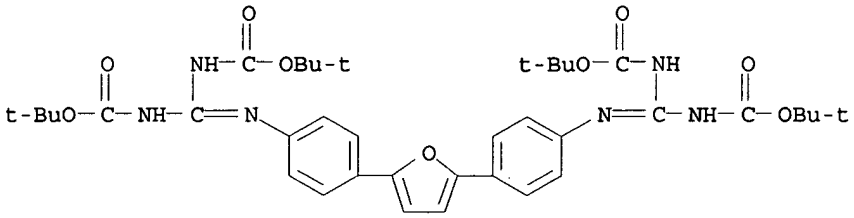
●2 HCl

RN 347190-98-1 HCAPLUS
CN Guanidine, N,N'''-[2,5-furandiylbis(3,5-dimethyl-4,1-phenylene)]bis-, dihydrochloride (9CI) (CA INDEX NAME)

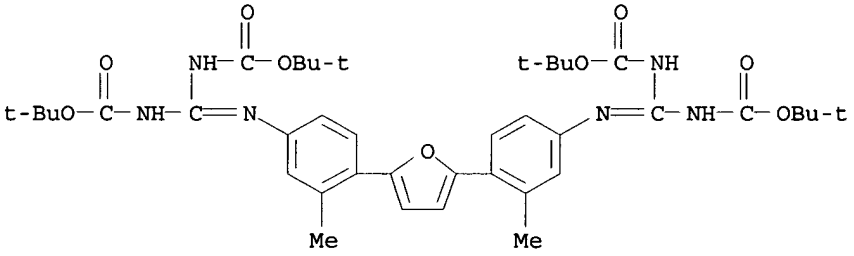


●2 HCl

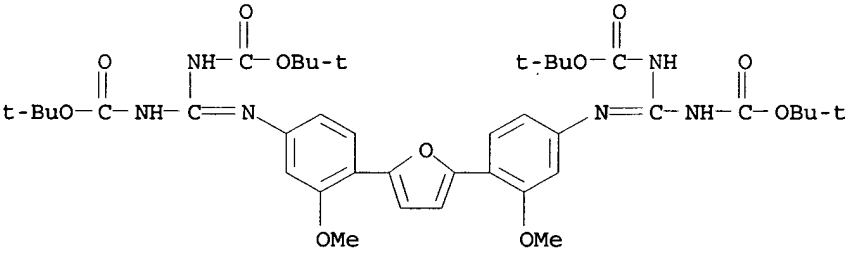
IT **347190-87-8P 347190-88-9P 347190-89-0P**
347190-90-3P 347190-91-4P 347190-92-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bis(guanidinoaryl)- and bis(amidinoaryl)furans as antifungal and antituberculosis agents)
RN 347190-87-8 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenenitrilomethanetetrayl)]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



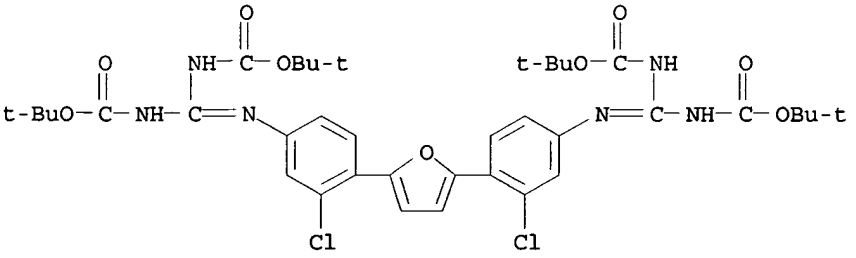
RN 347190-88-9 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3-methyl-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 347190-89-0 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3-methoxy-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

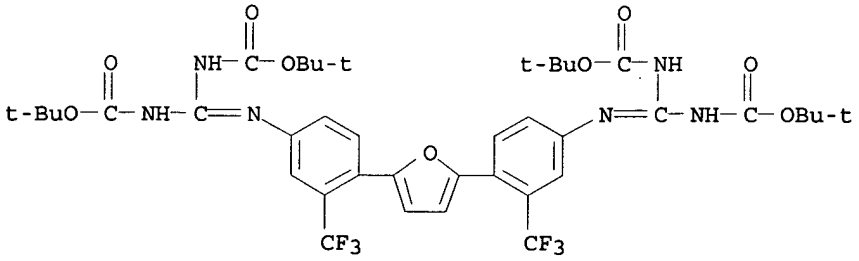


RN 347190-90-3 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3-chloro-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

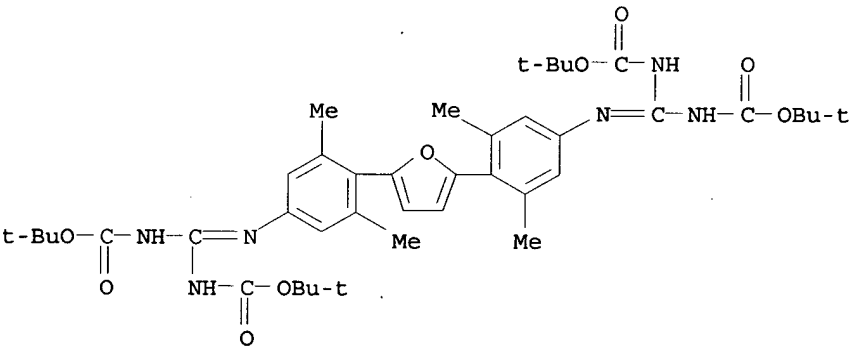


RN 347190-91-4 HCAPLUS

CN Carbamic acid, [2,5-furandiylbis[[3-(trifluoromethyl)-4,1-phenylene]nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 347190-92-5 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis[(3,5-dimethyl-4,1-phenylene)nitrilomethanetetrayl]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



CC 27-6 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
ST fungicidal antituberculostatic amidinophenylfuran; substituent effect DNA binding affinity arylfuran cationic; arylfuran amidino guanidino **antimicrobial** agent prepn; furan guanidinophenyl prepn; amidinophenyl furan imino prepn
IT **347190-93-6P 347190-94-7P 347190-95-8P**
347190-96-9P 347190-97-0P 347190-98-1P
347191-00-8P 347191-03-1P 347191-05-3P 347191-06-4P
347191-08-6P 347191-11-1P 347191-13-3P 347191-15-5P
347191-17-7P 347191-19-9P 347191-21-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of bis(guanidinoaryl)- and bis(amidinoaryl)furans as antifungal and antituberculosis agents)
IT 53715-17-6P 56297-30-4P 251577-90-9P 347190-78-7P
347190-79-8P 347190-80-1P 347190-81-2P 347190-82-3P
347190-83-4P 347190-84-5P 347190-85-6P 347190-86-7P
347190-87-8P 347190-88-9P 347190-89-0P
347190-90-3P 347190-91-4P 347190-92-5P
347190-99-2P 347191-01-9P 347191-02-0P 347191-04-2P
347191-07-5P 347191-09-7P 347191-10-0P 347191-12-2P
347191-14-4P 347191-16-6P 347191-18-8P 347191-20-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bis(guanidinoaryl)- and bis(amidinoaryl)furans as

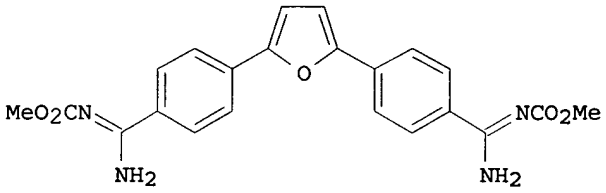
antifungal and antituberculosis agents)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:50472 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 134:120935
TITLE: Prodrugs for **antimicrobial** amidines
INVENTOR(S): Boykin, David W.; Rahmathullah, M. Syed; Tidwell, Richard R.; Hall, James E.
PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001003685	A2	20010118	WO 2000-US18499	2000 0706
WO 2001003685	A3	20020711		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2377902	AA	20010118	CA 2000-2377902	2000 0706
EP 1242059	A2	20020925	EP 2000-950293	2000 0706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003504329	T2	20030204	JP 2001-508966	2000 0706
AU 779923	B2	20050217	AU 2000-63416	2000 0706
AU 2000063416	A5	20010130		
US 6486200	B1	20021126	US 2000-612138	2000 0707
US 2002019437	A1	20020214	US 2001-918787	2001 0731
US 6503940	B2	20030107		
US 2003092755	A1	20030515	US 2002-208947	2002 0730
US 6649652	B2	20031118		
PRIORITY APPLN. INFO.:			US 1999-142826P P	1999

		0708
WO 2000-US18499	W	2000 0706
US 2000-612138	A3	2000 0707
US 2001-918787	B3	2001 0731

OTHER SOURCE(S): MARPAT 134:120935
GI



I

AB A methods of treating an infection comprises administering a therapeutically effective amount of a bis(amidinophenyl)furan. E.g., I was prepared along with 10 other similar compds. and showed in vivo activity against Pneumocystis carinii.

IT **73819-26-8P 247032-10-6P 247032-11-7P**
247032-12-8P 247032-13-9P 247032-14-0P
247032-15-1P 247032-16-2P 247032-17-3P
247032-18-4P 247032-19-5P 247032-22-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prodrugs for **antimicrobial** amidines)

RN 73819-26-8 HCAPLUS
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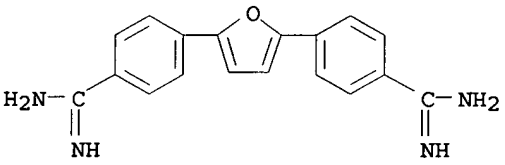

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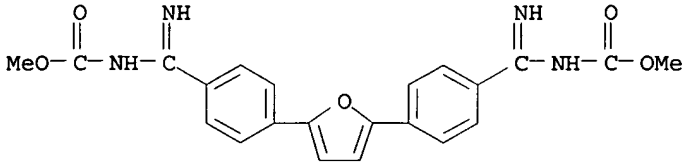
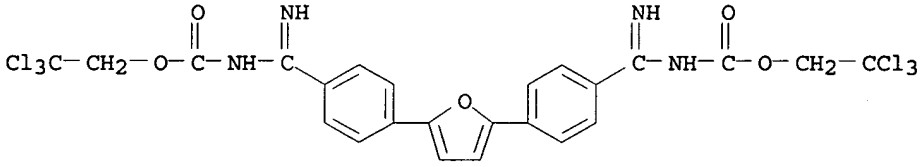
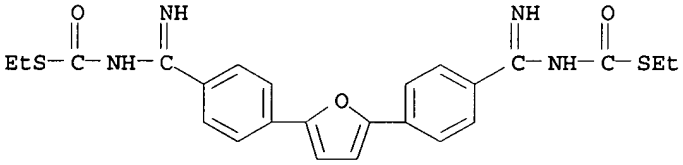


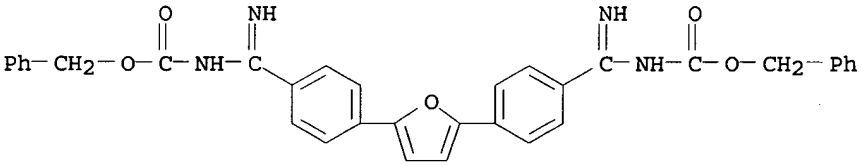
RN 247032-11-7 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)



RN 247032-12-8 HCAPLUS
CN Carbamothioic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, S,S-diethyl ester (9CI) (CA INDEX NAME)

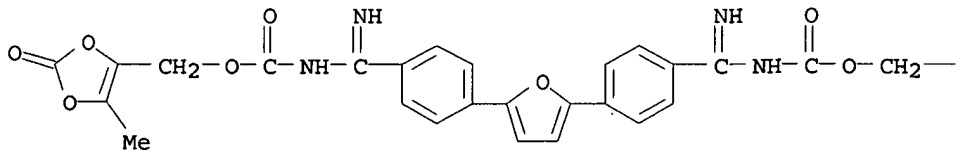


RN 247032-13-9 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

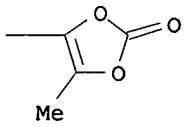


RN 247032-14-0 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis[(5-methyl-2-oxo-1,3-dioxol-4-yl)methyl] ester (9CI) (CA INDEX NAME)

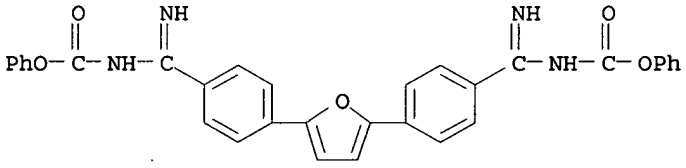
PAGE 1-A



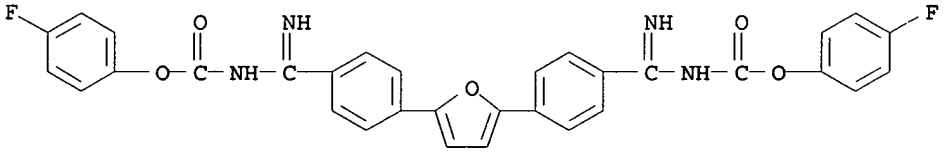
PAGE 1-B



RN 247032-15-1 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, diphenyl ester (9CI) (CA INDEX NAME)

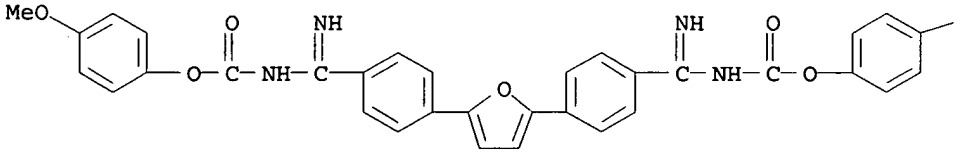


RN 247032-16-2 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-fluorophenyl) ester (9CI) (CA INDEX NAME)



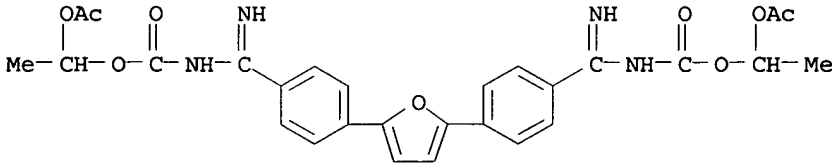
RN 247032-17-3 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-methoxyphenyl) ester (9CI) (CA INDEX NAME)

PAGE 1-A

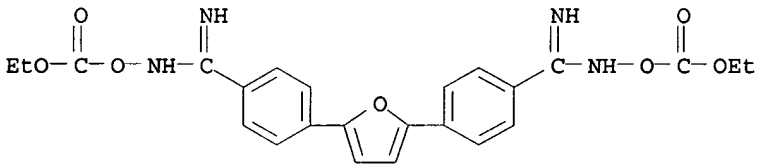


PAGE 1-B

RN 247032-18-4 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis[1-(acetyloxy)ethyl] ester (9CI) (CA INDEX NAME)



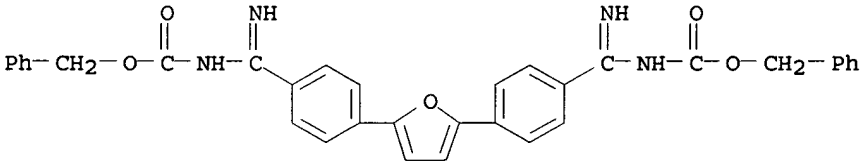
RN 247032-19-5 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[(ethoxycarbonyl)oxy]- (9CI) (CA INDEX NAME)



RN 247032-22-0 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(phenylmethyl) ester, (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

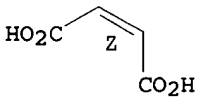
CRN 247032-13-9
CMF C34 H28 N4 O5



CM 2

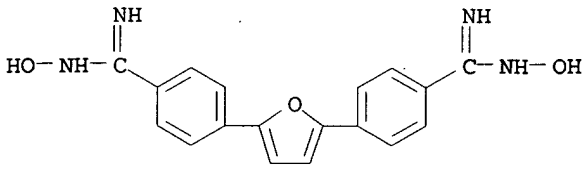
CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



IT **186953-55-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prodrugs for **antimicrobial** amidines)
RN 186953-55-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 27
ST amidinophenyl furan prodrug **antimicrobial**
IT **Antimicrobial** agents
Infection
Pneumocystis carinii
Pneumonia
(prodrugs for **antimicrobial** amidines)
IT **Drug delivery** systems
(prodrugs; prodrugs for **antimicrobial** amidines)
IT **73819-26-8P 247032-10-6P 247032-11-7P**
247032-12-8P 247032-13-9P 247032-14-0P
247032-15-1P 247032-16-2P 247032-17-3P
247032-18-4P 247032-19-5P 247032-22-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prodrugs for **antimicrobial** amidines)
IT 68-12-2, Dmf, processes 75-05-8, Acetonitrile, processes 109-99-9, Thf, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(prodrugs for **antimicrobial** amidines)
IT 100-02-7, 4-Nitrophenol, reactions 150-76-5, 4-Methoxyphenol 371-41-5, 4-Fluorophenol 501-53-1, Benzyl chloroformate 541-41-3, Ethyl chloroformate 2941-64-2 7087-68-5, Diisopropylethylamine 7693-41-6, 4-Methoxyphenyl chloroformate 7693-46-1, 4-Nitrophenyl chloroformate 17341-93-4, 2,2,2-Trichloroethyl chloroformate 37830-90-3, 4,5-Dimethyl-1,3-dioxol-2-one 38377-38-7, 4-Fluorophenyl chloroformate 50893-53-3, 1-Chloroethyl chloroformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(prodrugs for **antimicrobial** amidines)
IT 102-09-0P, Diphenyl carbonate 5676-71-1P, Bis(4-methoxyphenyl) carbonate 6132-45-2P, Ethyl 4-nitrophenyl carbonate 13795-24-9P, Benzyl p-nitrophenyl carbonate 17175-16-5P, Methyl 4-nitrophenyl carbonate 19394-12-8P 80715-22-6P 91526-17-9P 91526-18-0P 101623-68-1P 101623-69-2P, 1-Chloroethyl 4-nitrophenyl carbonate 173604-87-0P **186953-55-9P** 247032-21-9P 320343-87-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prodrugs for **antimicrobial** amidines)

L42 ANSWER 30 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:84606 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 132:117565
TITLE: Pentamidine and analogs as imidazoline receptor-binding compounds, and library

screening method

INVENTOR(S): Tidwell, Richard R.; Hall, James E.; Wood, Dorothy H.

PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA

SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004893	A2	20000203	WO 1999-US14428	19990625
WO 2000004893	A3	20000629		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6635668	B1	20031021	US 1998-120584	19980722
CA 2338279	AA	20000203	CA 1999-2338279	19990625
AU 9948327	A1	20000214	AU 1999-48327	19990625
AU 766814	B2	20031023		
EP 1097382	A2	20010509	EP 1999-931916	19990625
R: CH, DE, FR, GB, IT, LI				
JP 2002527357	T2	20020827	JP 2000-560886	19990625
US 2004082663	A1	20040429	US 2003-663879	20030916
AU 2004200272	A1	20040219	AU 2004-200272	20040123

PRIORITY APPLN. INFO.:	US 1998-120584	A	19980722
	WO 1999-US14428	W	19990625

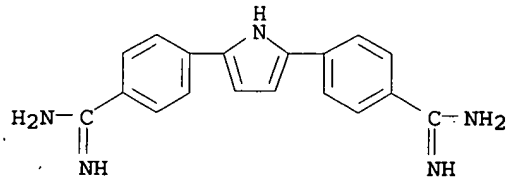
OTHER SOURCE(S): MARPAT 132:117565

AB Pentamidine and analogs thereof have activity as imidazoline receptor binding compds. A method of binding the imidazoline receptor comprises contacting a bis-benzene to the imidazoline receptor in an amount effective to bind to the receptor, wherein the bis-benzene contains at least one amidine group (e.g., one or two). The contacting step may be carried out in vivo or in vitro.

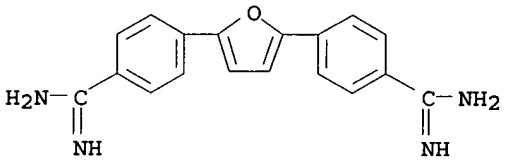
Contacting may be carried out with individual active compds. or with libraries of active compds.

IT **66639-43-8**, DB 262 **73819-26-8**, DB 75
73819-28-0, DB 351 **173420-56-9**, DB 181
192525-51-2, DB 244
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pentamidine and analogs as imidazoline receptor-binding compds., and library screening method)

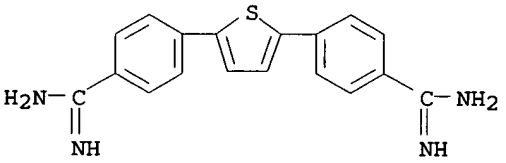
RN 66639-43-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(1H-pyrrole-2,5-diyl)bis- (9CI) (CA INDEX NAME)



RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 73819-28-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-thiophenediyl)bis- (9CI) (CA INDEX NAME)



RN 173420-56-9 HCAPLUS
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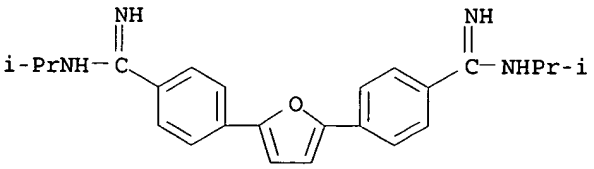
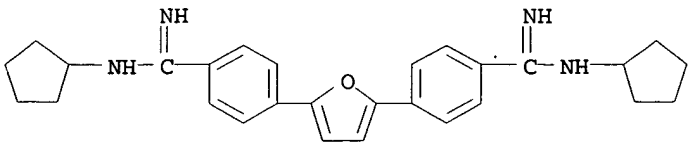


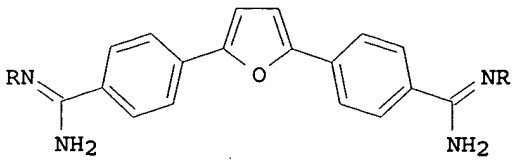
RN 192525-51-2 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-cyclopentyl- (9CI) (CA INDEX NAME)



IC ICM A61K031-00
CC 1-12 (Pharmacology)
Section cross-reference(s): 25
IT **Antimicrobial** agents
Combinatorial library
Drug screening
Lipophilicity
Pneumocystis carinii
QSAR (structure-activity relationship)
Structure-activity relationship
(pentamidine and analogs as imidazoline receptor-binding compds., and library screening method)
IT 26130-55-2, FS 117 31066-05-4, FS 104 35872-76-5, KAO 011 56806-89-4, MC 96 56807-02-4, MC 97c 57323-76-9, FS 44 **66639-43-8**, DB 262 67833-71-0, FS 113 **73819-26-8** , DB 75 **73819-28-0**, DB 351 74733-75-8, BABIM 80498-71-1, DB 60 80498-74-4, DB 103 100562-53-6, BABB 148344-24-5, BIBB 163228-13-5, DB 183 **173420-56-9**, DB 181 **192525-51-2**, DB 244 200878-32-6, KAO 111 200878-40-6, DAP 092 256459-03-7, DB 205
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pentamidine and analogs as imidazoline receptor-binding compds., and library screening method)

L42 ANSWER 31 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:562085 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 131:299327
TITLE: Prodrugs for Amidines: Synthesis and Anti-Pneumocystis carinii Activity of Carbamates of 2,5-Bis(4-amidinophenyl)furan
AUTHOR(S): Rahmathullah, Syed M.; Hall, James Edwin; Bender, Brendan C.; McCurdy, Donald R.; Tidwell, Richard R.; Boykin, David W.
CORPORATE SOURCE: Department of Chemistry and Center for Biotechnology and Drug Design, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Journal of Medicinal Chemistry (1999), 42(19), 3994-4000
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:299327
GI



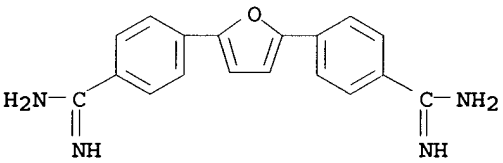
I

AB Syntheses of several carbamate analogs of 2,5-bis(4-amidinophenyl)furan (I, R = H) under mild conditions and their evaluation as prodrugs against Pneumocystis carinii pneumonia (PCP) in an immunosuppressed rat model are described. Thus, nine new bis(carbamates) of bis(amidine) I [R = MeO2C (II), Cl3CCH2O2C (III), EtSCO (IV), PhCH2O2C (V), (4-methyl-2-oxo-1,3-dioxol-4-en-5-yl)methoxycarbonyl (VI), PhO2C (VII), 4-FC6H4O2C (VIII), 4-MeOC6H4O2C (IX), AcOCHMeO2C (X)] and a bis(carbonate) [R = EtOC(O)O (XI)] have been synthesized and evaluated. The in vivo results show that VIII and IX had the best anti-PCP activity by both i.v. and oral administration. Compds. III-VII were also more active than the parent drug I on oral administration. The acute toxicity usually exhibited by the parent amidine I at 22 μmol/kg/day on i.v. administration has been significantly reduced by the prodrug modifications, with the exception of compound X which exhibited some toxicity. The syntheses of several aryl alkyl and diaryl carbonates as efficient reagents for the preparation of carbamate derivs. from bis(arylamidines) are also described.

IT **73819-26-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation and anti-Pneumocystis carinii activity of carbamates of bis(amidinophenyl)furan prepared from aryl alkyl and diaryl carbonates)

RN 73819-26-8 HCAPLUS

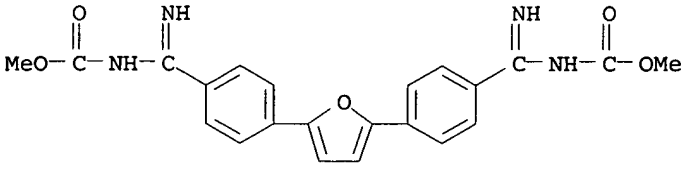
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



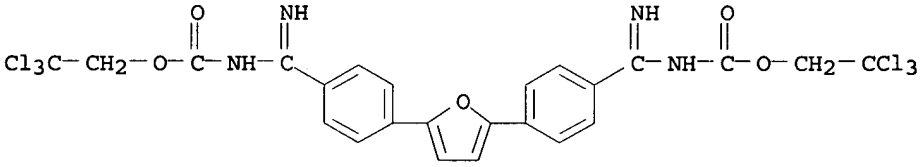
IT **247032-10-6P 247032-11-7P 247032-12-8P**
247032-13-9P 247032-14-0P 247032-15-1P
247032-16-2P 247032-17-3P 247032-18-4P
247032-19-5P 247032-22-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anti-Pneumocystis carinii activity of carbamates of bis(amidinophenyl)furan prepared from aryl alkyl and diaryl carbonates)

RN 247032-10-6 HCAPLUS

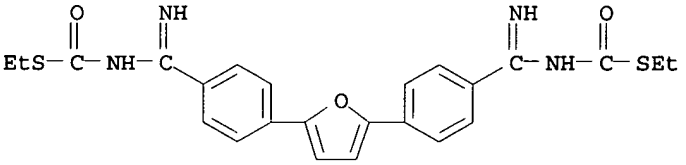
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, dimethyl ester (9CI) (CA INDEX NAME)



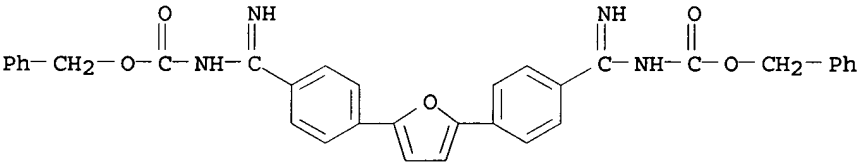
RN 247032-11-7 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(2,2,2-trichloroethyl) ester (9CI) (CA INDEX NAME)



RN 247032-12-8 HCAPLUS
CN Carbamothioic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, S,S-diethyl ester (9CI) (CA INDEX NAME)

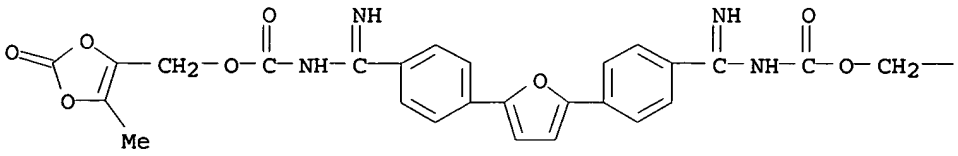


RN 247032-13-9 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

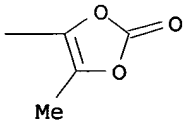


RN 247032-14-0 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis[(5-methyl-2-oxo-1,3-dioxol-4-yl)methyl] ester (9CI) (CA INDEX NAME)

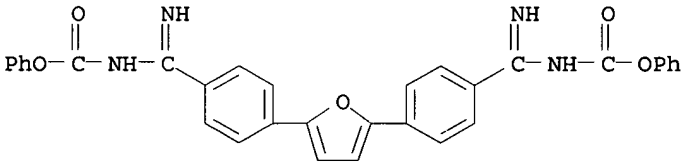
PAGE 1-A



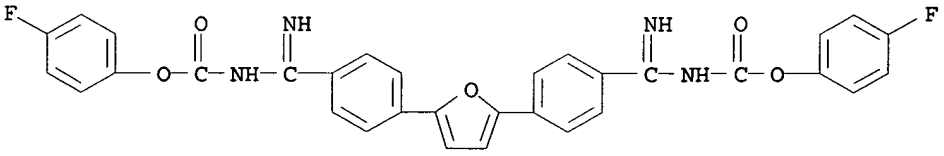
PAGE 1-B



RN 247032-15-1 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, diphenyl ester (9CI) (CA INDEX NAME)

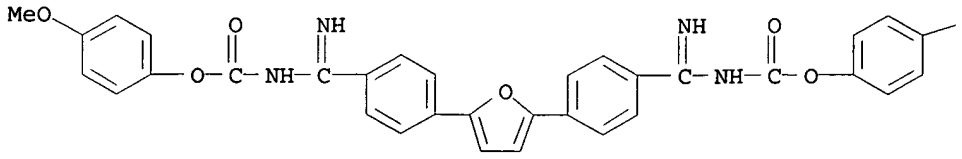


RN 247032-16-2 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-fluorophenyl) ester (9CI) (CA INDEX NAME)



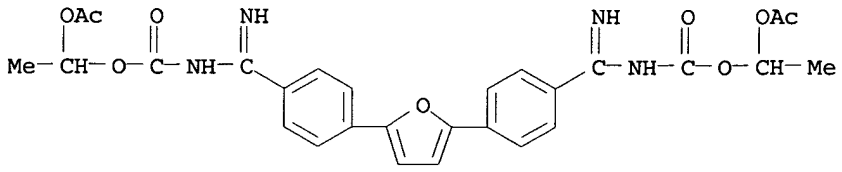
RN 247032-17-3 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(4-methoxyphenyl) ester (9CI) (CA INDEX NAME)

PAGE 1-A

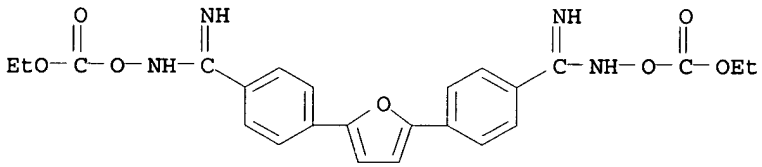


PAGE 1-B

RN 247032-18-4 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis[1-(acetyloxy)ethyl] ester (9CI) (CA INDEX NAME)



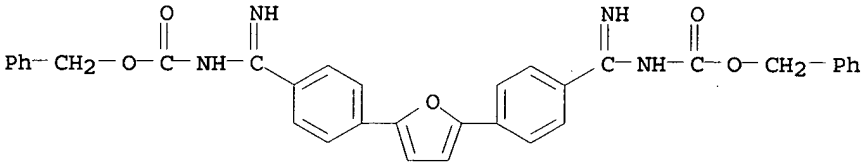
RN 247032-19-5 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[(ethoxycarbonyl)oxy]- (9CI) (CA INDEX NAME)



RN 247032-22-0 HCAPLUS
CN Carbamic acid, [2,5-furandiylbis(4,1-phenylenecarbonimidoyl)]bis-, bis(phenylmethyl) ester, (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

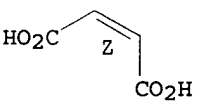
CRN 247032-13-9
CMF C34 H28 N4 O5



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

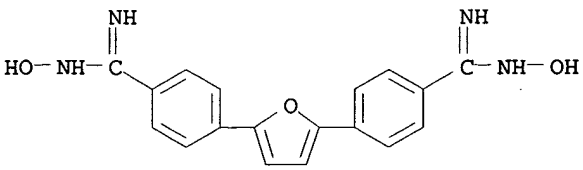


IT **186953-55-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and anti-Pneumocystis carinii activity of carbamates of

bis(amidinophenyl)furan prepared from aryl alkyl and diaryl carbonates)

RN 186953-55-9 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-hydroxy- (9CI) (CA INDEX NAME)



CC 27-6 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT **Drug delivery** systems
(prodrugs; preparation and anti-Pneumocystis carinii activity of carbamates of bis(amidinophenyl)furan prepared from aryl alkyl and diaryl carbonates)

IT **73819-26-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation and anti-Pneumocystis carinii activity of carbamates of bis(amidinophenyl)furan prepared from aryl alkyl and diaryl carbonates)

IT **247032-10-6P 247032-11-7P 247032-12-8P**
247032-13-9P 247032-14-0P 247032-15-1P
247032-16-2P 247032-17-3P 247032-18-4P
247032-19-5P 247032-22-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anti-Pneumocystis carinii activity of carbamates of bis(amidinophenyl)furan prepared from aryl alkyl and diaryl carbonates)

IT 79-22-1, Methyl chloroformate 501-53-1, Benzyl chloroformate 541-41-3, Ethyl chloroformate 1885-14-9 2941-64-2, S-Ethyl chlorothioformate 7693-41-6, 4-Methoxyphenyl chloroformate 7693-46-1, 4-Nitrophenyl chloroformate 17341-93-4, 2,2,2-Trichloroethyl chloroformate 37830-90-3 38377-38-7, 4-Fluorophenyl chloroformate 50893-53-3, 1-Chloroethyl chloroformate 91526-18-0 **186953-55-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and anti-Pneumocystis carinii activity of carbamates of bis(amidinophenyl)furan prepared from aryl alkyl and diaryl carbonates)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 32 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:502766 HCAPLUS <<LOGINID::20060221>>

DOCUMENT NUMBER: 131:153725

TITLE: Small molecule inhibition of RNA/ligand binding

INVENTOR(S): Green, Michael R.; Zapp, Maria L.

PATENT ASSIGNEE(S): University of Massachusetts Medical Center, USA

SOURCE: U.S., 14 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

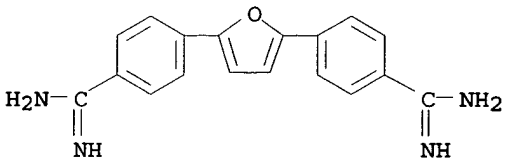
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5935776	A	19990810	US 1995-399378	19950302
US 5534408	A	19960709	US 1993-126236	19930924
PRIORITY APPLN. INFO.:			US 1992-965341 B2	19921023
			US 1993-126236 A2	19930924

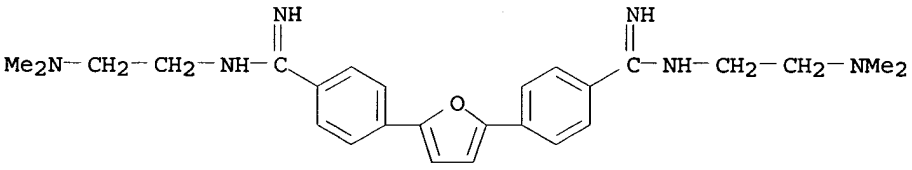
AB A method is disclosed for the inhibition of binding of a ligand to an RNA, the inhibition being mediated by a small organic mol. that binds to the RNA, thereby inhibiting ligand binding. The invention is particularly directed to the interaction of the Rev protein of HIV with the Rev-responsive element (RRE) present in HIV-derived mRNA mols. A preferred class of small organic mols. are compds. exemplified by 2,5-Bis[4-(2-N,N-dimethylaminopropylamidino)phenyl]furan.

IT **73819-26-8P 166601-09-8P 236098-04-7P 236098-05-8P 236098-06-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(small mol. inhibition of RNA/ligand binding)

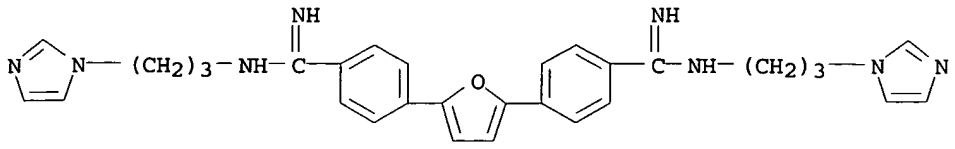
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 166601-09-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)

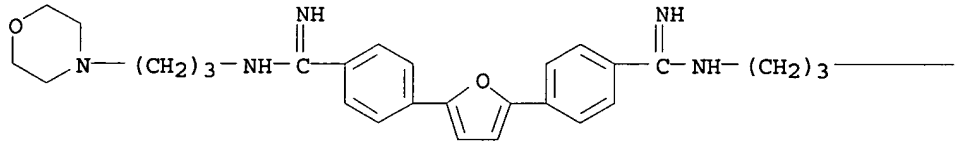


RN 236098-04-7 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)

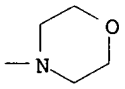


RN 236098-05-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)

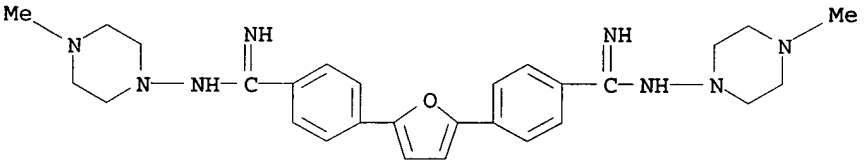
PAGE 1-A



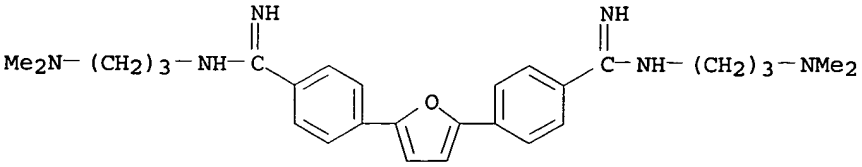
PAGE 1-B



RN 236098-06-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



IT **166601-11-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small mol. inhibition of RNA/ligand binding)
RN 166601-11-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



IC ICM C12Q001-70
ICS C12Q001-68; A01N043-08; A61K031-34
INCL 435005000

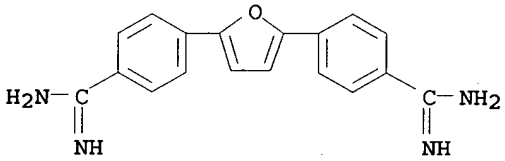
CC 1-5 (Pharmacology)
Section cross-reference(s): 27, 28, 63
IT Antiviral agents
Drug delivery systems
Human immunodeficiency virus
Molecular association
RNA sequences
Retroviridae
Structure-activity relationship
(small mol. inhibition of RNA/ligand binding)
IT **73819-26-8P 166601-09-8P 236098-04-7P**
236098-05-8P 236098-06-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(small mol. inhibition of RNA/ligand binding)
IT 119-04-0, Neomycin B 1403-66-3, Gentamicin 3947-65-7, Neamine 4696-76-8, Kanamycin B 25546-65-0, Ribostamycin 32385-11-8 32986-56-4, Tobramycin 36441-41-5, Lividomycin A 37517-28-5, Amikacin **166601-11-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small mol. inhibition of RNA/ligand binding)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 33 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:363786 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 131:125080
TITLE: Relationships between topoisomerase II inhibition, sequence-specificity and DNA binding mode of dicationic diphenylfuran derivatives
AUTHOR(S): Bailly, Christian; Dassonneville, Laurent; Carrasco, Carolina; Lucas, Delphine; Kumar, Arvind; Boykin, David W.; Wilson, W. David
CORPORATE SOURCE: INSERM U-524 and Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCL, Lille, 59045, Fr.
SOURCE: Anti-Cancer Drug Design (1999), 14(1), 47-60
CODEN: ACDDEA; ISSN: 0266-9536
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Four diphenylfuran derivs. possessing different dicationic terminal side chains were used to investigate sequence-specific binding to DNA and poisoning of human topoisomerase II. Footprinting expts. with a range of DNA substrates attest that all four drugs bind selectively to AT-rich sequences in DNA. However, the quant. anal. of the footprinting profiles reveals significant differences in terms of AT-selectivity according to the nature of the basic side chains. Furimidazoline (DB60) shows a reduced capacity to interact selectively with A·T tetrads compared with furamidine (DB75) and the 3-pentyl-substituted diamidine analog DB226. DB244, for which the two amidine ends are substituted with a cyclopentyl group, exhibits the most pronounced AT specificity. It binds tightly to sites composed of at least four adjacent AT base pairs, such as 5'-TAAT, AATT and TTTT. At low concns. (<2 μM) DB60 is also capable of forming stable complexes with AT sites but at higher concns. the binding becomes totally non-specific due to addnl. intercalation of drug mols. into GC-rich sequences. Nevertheless, DB60 is the only drug is the series which stabilizes DNA-topoisomerase II covalent

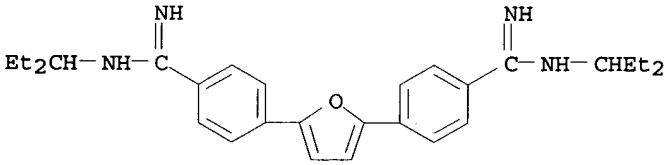
complexes. This compound effectively promotes DNA cleavage by topoisomerase II whereas DB75, DB226 and DB244 have practically no effect. The topoisomerase II poisoning activity of DB60 correlates with its ability to intercalate into GC sites in DNA whereas the three other diphenylfurans essentially behave as typical AT-selective minor groove binders. The study suggests that the **antimicrobial** activity of the diphenylfurans, which are active against the Pneumocystis carinii pathogen (PCP), depends essentially on their capacity to recognize AT-rich DNA sequences rather than their ability to interfere with topoisomerase II. In contrast, the cytotoxicity of drugs like DB60 would be connected with the formation of intercalation complexes and the stimulation of DNA cleavage by human topoisomerase II.

IT **73819-26-8**, DB 75 **179118-17-3**, DB 226
192525-51-2, DB 244
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(relationships between topoisomerase II inhibition, sequence-specificity and DNA binding mode of dicationic diphenylfuran derivs.)

RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 179118-17-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-ethylpropyl)- (9CI) (CA INDEX NAME)



RN 192525-51-2 HCAPLUS
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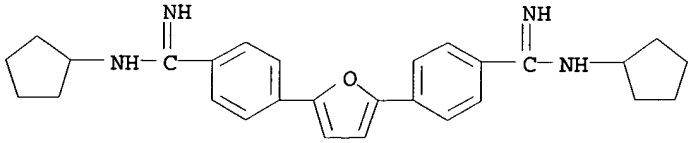


CC 1-6 (Pharmacology)
ST dicationic diphenylfuran topoisomerase II inhibition antitumor **antimicrobial**; DNA binding dicationic diphenylfuran deriv DB60
IT **Antimicrobial** agents

Antitumor agents
Pneumocystis carinii carinii
(relationships between topoisomerase II inhibition, sequence-specificity and DNA binding mode of dicationic diphenylfuran derivs.)

IT 26569-47-1D, Diphenylfuran, dicationic derivs. **73819-26-8**, DB 75 80498-71-1, DB 60 **179118-17-3**, DB 226 **192525-51-2**, DB 244
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(relationships between topoisomerase II inhibition, sequence-specificity and DNA binding mode of dicationic diphenylfuran derivs.)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 34 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:785675 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 130:32999
TITLE: Benzamidoxime prodrugs as antipneumocystic agents
INVENTOR(S): Hall, James E.; Tidwell, Richard R.; Boykin, David W.
PATENT ASSIGNEE(S): Georgia State University Research Foundation Inc., USA; The University of North Carolina At Chapel Hill
SOURCE: U.S., 17 pp., Cont.-in-part of U.S. 5,723,495. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

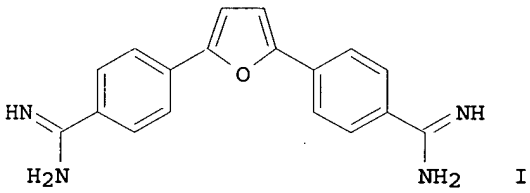
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5843980	A	19981201	US 1996-751171	1996 1115
US 5723495	A	19980303	US 1995-558716	1995 1116
CA 2237650	AA	19970522	CA 1996-2237650	1996 1115
EP 1561463	A2	20050810	EP 2005-5110	1996 1115
R: CH, DE, ES, FR, GB, IT, LI				
ES 2241008	T3	20051016	ES 1996-942773	1996 1115
US 6025398	A	20000215	US 1998-127317	1998 0731
US 6214883	B1	20010410	US 2000-477390	2000 0104
AU 764937	B2	20030904	AU 2000-62473	2000 1004
US 2001044468	A1	20011122	US 2001-759664	2001 0112
US 6423737	B2	20020723		

PRIORITY APPLN. INFO.:

US 1995-558716	A2	1995 1116
AU 1997-11605	A3	1996 1115
EP 1996-942773	A3	1996 1115
US 1996-751171	A3	1996 1115
US 1998-127317	A3	1998 0731
US 2000-477390	A3	2000 0104

OTHER SOURCE(S): MARPAT 130:32999

GI



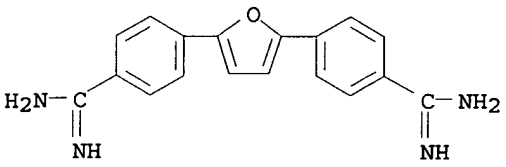
I

AB A method of treating Pneumocystis carinii pneumonia in a subject in need of such treatment is disclosed. The method comprises orally administering to the subject bis-benzamidoximes, such as I, which exhibited significant activity in infected rats (the anti-Pneumocystis value was expressed in percent of lung cysts in the treatment group vs. control group). The method of the present invention may alternatively comprise i.v. administering to the subject an active compound as disclosed herein. Pharmaceutical formulations and active compds. useful in the practice of the present invention are also disclosed.

IT **73819-26-8P 186953-55-9P 186953-56-0P 186953-57-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzamidoxime prodrugs as antipneumocystic agents)

RN 73819-26-8 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 186953-55-9 HCAPLUS
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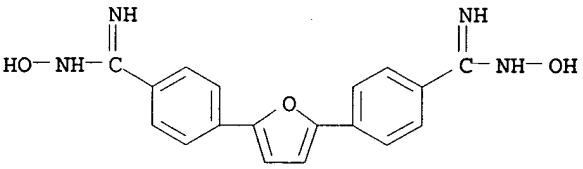

RN 186953-56-0 HCAPLUS
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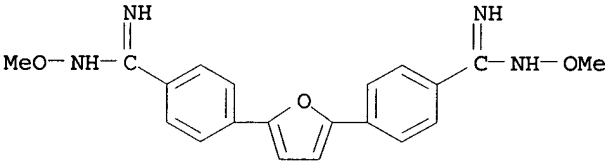

RN 186953-57-1 HCAPLUS
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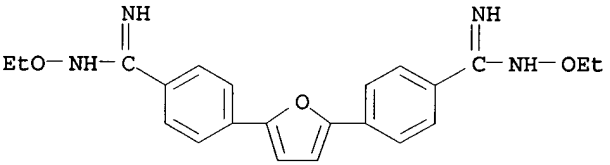
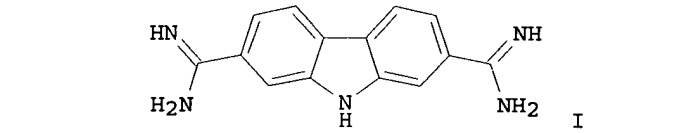


IC ICM A61K031-34
ICS A61K031-38; C07D307-52; C07D333-20
INCL 514438000
CC 1-5 (Pharmacology)
IT **Drug delivery** systems
(prodrugs; preparation of benzamidoxime prodrugs as antipneumocystic agents)
IT 104-32-5P **73819-26-8P** 124076-61-5P 124076-65-9P
186953-55-9P 186953-56-0P 186953-57-1P
190958-04-4P 190958-07-7P 190958-13-5P 190958-17-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzamidoxime prodrugs as antipneumocystic agents)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 35 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:664986 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 130:22621
TITLE: In vitro antifungal activities of a series of dication-substituted carbazoles, furans, and benzimidazoles
AUTHOR(S): Del Poeta, Maurizio; Schell, Wiley A.; Dykstra, Christine C.; Jones, Susan K.; Tidwell, Richard R.; Kumar, Arvind; Boykin, David W.; Perfect, John R.
CORPORATE SOURCE: Department of Medicine, Division of Infectious Diseases and International Health, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(10), 2503-2510
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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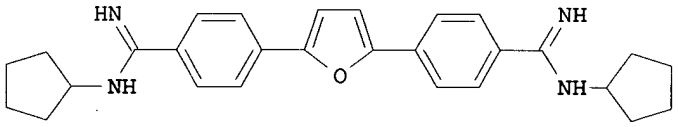

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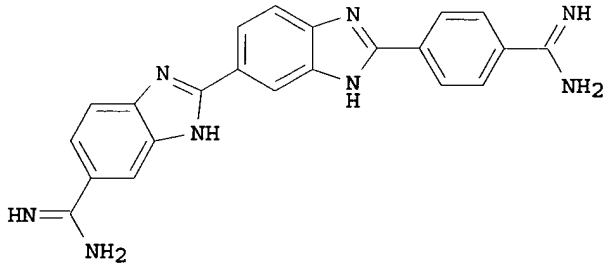


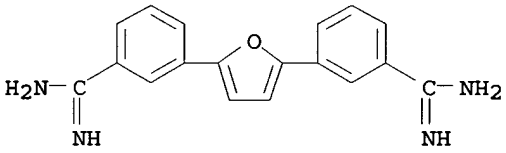
III

AB Aromatic dicationic compds. possess **antimicrobial** activity against a wide range of eucaryotic pathogens, and in the present study an examination of the structures-functions of a series of compds. against fungi was performed. Sixty-seven dicationic mols. were screened for their inhibitory and fungicidal activities against Candida albicans and Cryptococcus neoformans. The MICs of a large number of compds. were comparable to those of the standard antifungal drugs amphotericin B and fluconazole. Unlike fluconazole, potent inhibitory compds. in this series were found to have excellent fungicidal activities. Broad-spectrum activities were observed for the carbazole I, the furan II, and the benzimidazole III. The MIC of III, one of the most potent compds., against C. albicans was

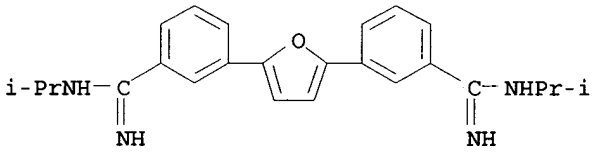
0.39 μg/mL, and it was the most potent compound against C. neoformans (MIC, ≤0.09 μg/mL). Selected compds. were also found to be active against Aspergillus fumigatus, Fusarium solani, Candida species other than C. albicans, and fluconazole-resistant strains of C. albicans and C. neoformans. Since of these compds. have been safely given to animals, these classes of mols. have the potential to be developed as antifungal agents.

IT **216308-16-6P 216308-17-7P 216308-18-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in vitro antifungal activities of a series of dication-substituted carbazoles, furans, and benzimidazoles)

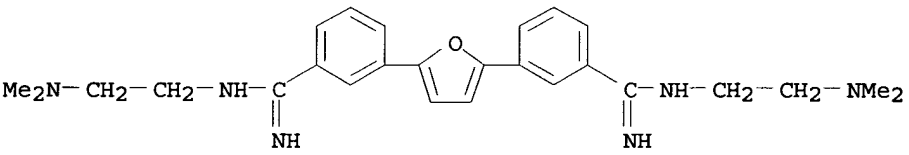
RN 216308-16-6 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 216308-17-7 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 216308-18-8 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis[N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



IT **73819-26-8 173420-56-9 173420-67-2**
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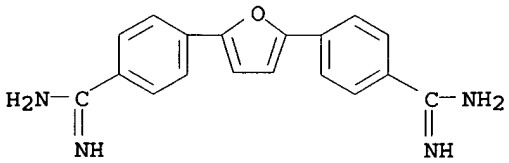
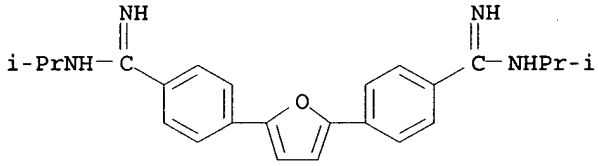
192525-50-1 192525-51-2 192525-52-3
199919-03-4 199919-06-7 216308-08-6
216308-09-7 216308-10-0 216308-11-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro antifungal activities of a series of dication-substituted carbazoles, furans, and benzimidazoles)

RN 73819-26-8 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 173420-56-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 173420-67-2 HCAPLUS
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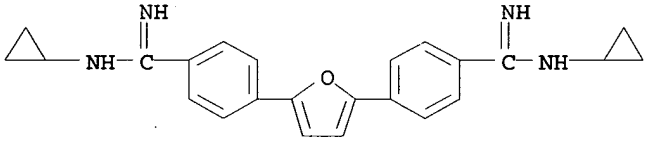
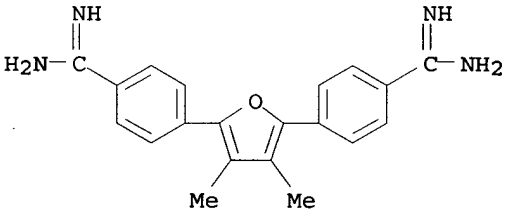
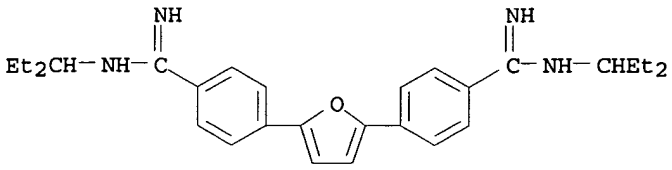


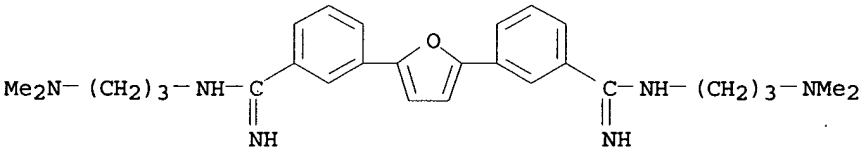
RN 179118-06-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3,4-dimethyl-2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



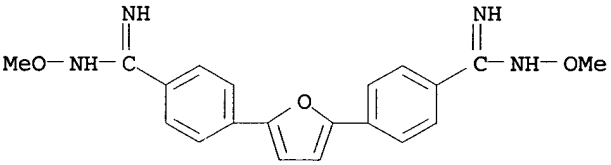
RN 179118-17-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-ethylpropyl)- (9CI) (CA INDEX NAME)



RN 186391-18-4 HCAPLUS
CN Benzenecarboximidamide, 3,3'-(2,5-furandiyl)bis[N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



RN 186953-56-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-methoxy- (9CI) (CA INDEX NAME)



RN 192525-48-7 HCAPLUS
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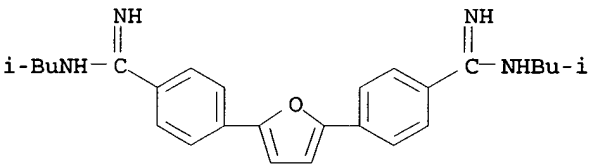

RN 192525-49-8 HCAPLUS
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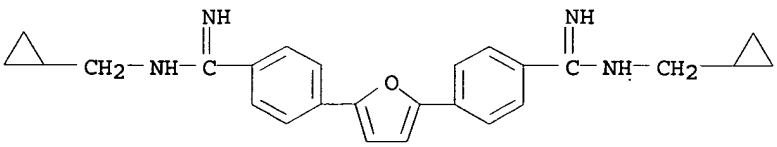

RN 192525-50-1 HCAPLUS
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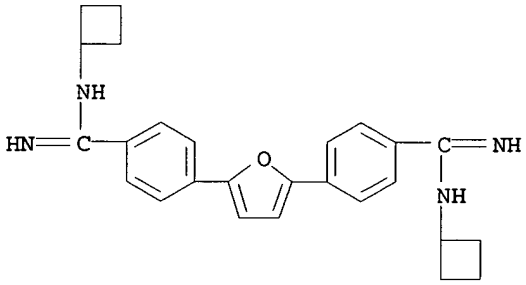
(9CI) (CA INDEX NAME)



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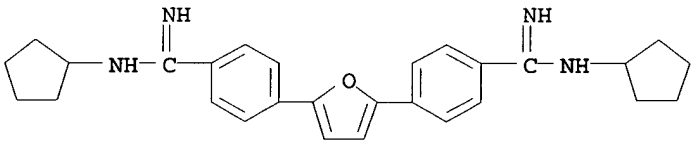
(9CI) (CA INDEX NAME)



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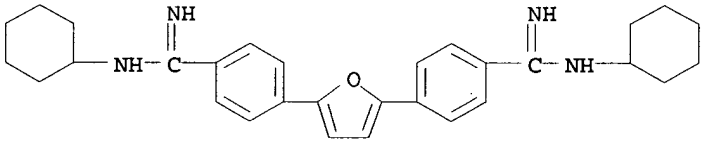
(9CI) (CA INDEX NAME)



RN 199919-03-4 HCAPLUS
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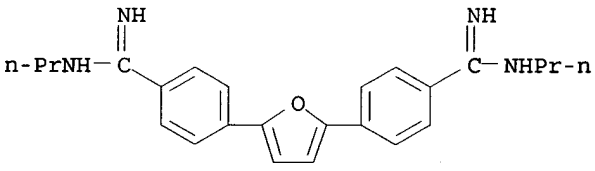
(CA INDEX NAME)



RN 199919-06-7 HCAPLUS
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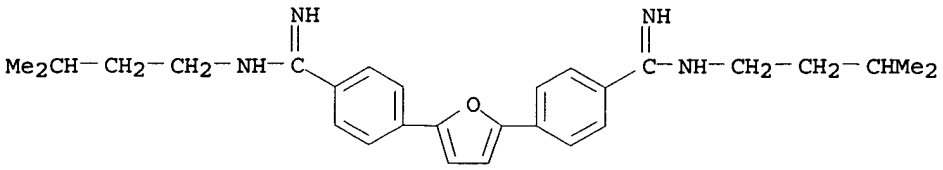
(9CI) (CA INDEX NAME)



RN 216308-08-6 HCAPLUS
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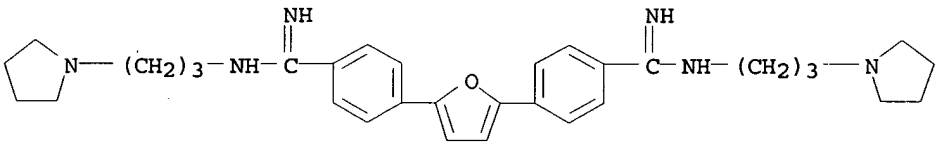

RN 216308-09-7 HCAPLUS
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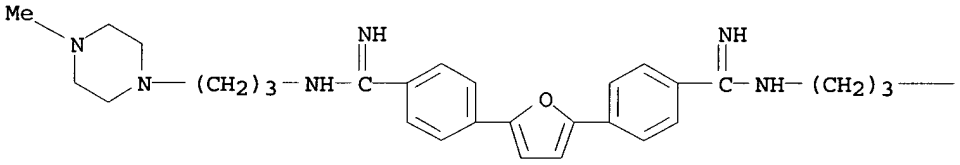
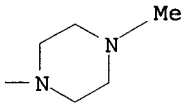
PAGE 1-A



PAGE 1-B



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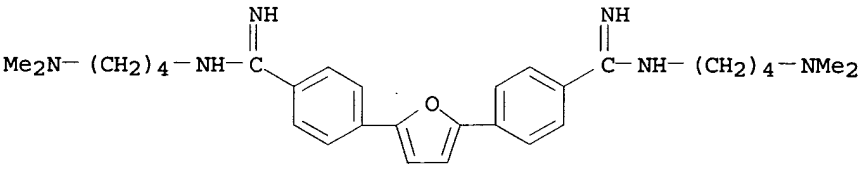

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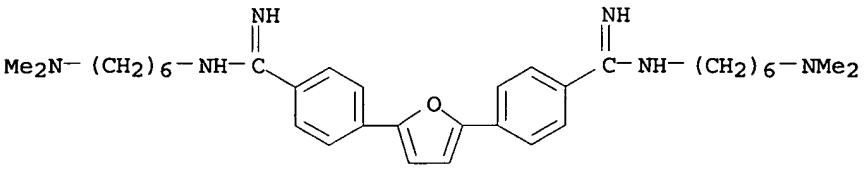

CC 10-1 (Microbial, Algal, and Fungal Biochemistry)
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216308-15-5P **216308-16-6P 216308-17-7P**
216308-18-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in vitro antifungal activities of a series of dication-substituted carbazoles, furans, and benzimidazoles)
IT 23491-44-3 40069-58-7 40069-59-8 66639-16-5
73819-26-8 95415-64-8 163228-07-7 163228-13-5
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163228-22-6 163228-23-7 **173420-56-9**
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200878-39-3 200878-40-6, 9H-Carbazole-2,7-dicarboximidamide
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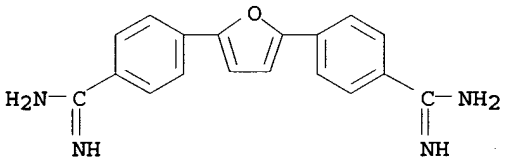
216308-21-3 216308-23-5 216308-25-7 216308-31-5
216308-32-6 216308-33-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro antifungal activities of a series of dication-substituted carbazoles, furans, and benzimidazoles)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 36 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:159773 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 128:241723
TITLE: Identification and characterization of an endo/exonuclease in Pneumocystis carinii that is inhibited by dicationic diarylfurans with efficacy against Pneumocystis pneumonia
AUTHOR(S): Hildebrandt, Ellen; Boykin, David W.; Kumar, Arvind; Tidwell, Richard R.; Dykstra, Christine C.
CORPORATE SOURCE: Department of Pathobiology, College of Veterinary Medicine, Auburn University, Auburn, AL, 36849, USA
SOURCE: Journal of Eukaryotic Microbiology (1998), 45(1), 112-121
CODEN: JEMIED; ISSN: 1066-5234
PUBLISHER: Society of Protozoologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dicationic diarylfurans and dicationic carbazoles are under

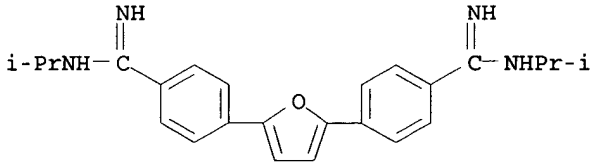
development as therapeutic agents against opportunistic infections. While their ability to bind to the minor groove of DNA has been established, the complete mechanism of action has not. We demonstrate here that an effective diarylfuran, 2,5-bis[4-(N-isopropylguanyl)phenyl]furan, inhibits an endo/exonuclease activity present in Pneumocystis carinii, Cryptococcus neoformans, Candida albicans, and Saccharomyces cerevisiae. This activity was purified from the particulate fraction of P. carinii. The enzyme requires Mg2+ or Mn2+, and shows preferences for single- over double-stranded DNA and for AT-rich over GC-rich domains. A panel of 12 dicationic diarylfurans and eight dicationic carbazoles, previously synthesized, were evaluated for inhibition of the purified nuclease and for efficacy against Pneumocystis pneumonia in rats. Among the diarylfurans, potency of nuclease inhibition, in vivo **antimicrobial** activity, and DNA binding strength were all strongly correlated ($p < 0.001$). These findings suggest that one target for **antimicrobial** action of the diarylfurans may be a nucleolytic or other event requiring unpairing of DNA strands. Dicationic carbazoles which were strong nuclease inhibitors all displayed anti-Pneumocystis activity in vivo, but there were also noninhibitory carbazoles with in vivo efficacy.

IT **73819-26-8 173420-56-9 173420-67-2 192525-48-7 192525-49-8 192525-50-1 192525-51-2 205122-83-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification and characterization of an endo/exonuclease in Pneumocystis carinii that is inhibited by dicationic diarylfurans with efficacy against Pneumocystis pneumonia)

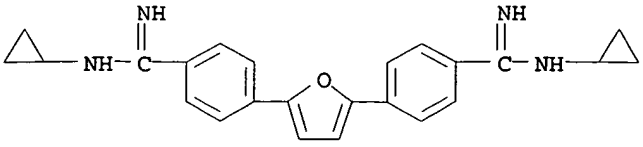
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



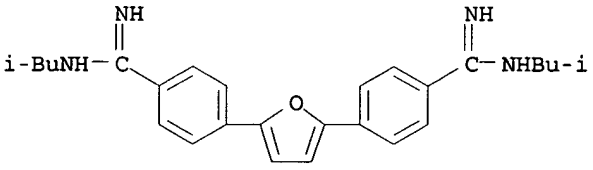
RN 173420-56-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)



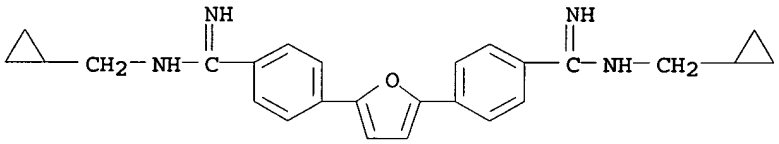
RN 173420-67-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-cyclopropyl- (9CI) (CA INDEX NAME)



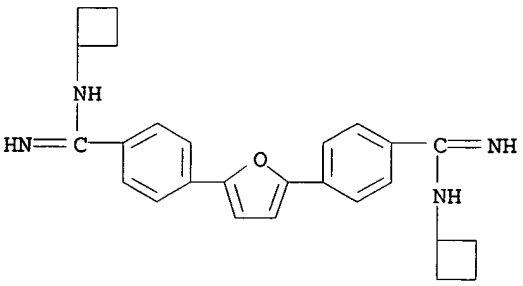
RN 192525-48-7 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(2-methylpropyl)- (9CI) (CA INDEX NAME)



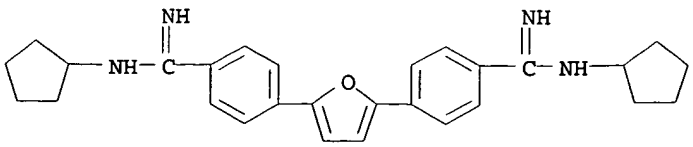
RN 192525-49-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(cyclopropylmethyl)- (9CI) (CA INDEX NAME)



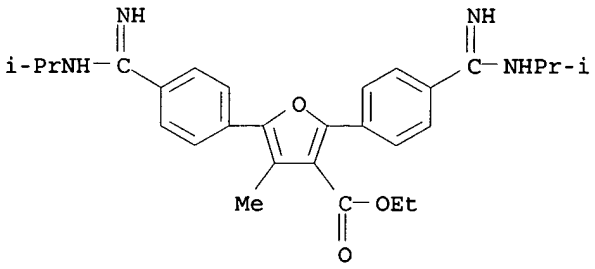
RN 192525-50-1 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-cyclobutyl- (9CI) (CA INDEX NAME)



RN 192525-51-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-cyclopentyl- (9CI) (CA INDEX NAME)



RN 205122-83-4 HCAPLUS
CN 3-Furancarboxylic acid, 2,5-bis[4-[imino[(1-methylethyl)amino]methyl]phenyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)



CC 10-5 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 1, 7
IT **73819-26-8** 80498-74-4 **173420-56-9**
173420-67-2 179118-03-7 **192525-48-7**
192525-49-8 **192525-50-1** **192525-51-2**
200878-37-1 200878-40-6, 9H-Carbazole-2,7-dicarboximidamide
205122-83-4 205122-84-5 205122-85-6 205122-86-7
205122-87-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification and characterization of an endo/exonuclease in Pneumocystis carinii that is inhibited by dicationic diarylfurans with efficacy against Pneumocystis pneumonia)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 37 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:464510 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 125:114460
TITLE: Preparation of furan derivatives for inhibition of pneumocystis carinii pneumonia, giardia lamblia, and cryptosporidium parvum
INVENTOR(S): Boykin, David W.; Dykstra, Christine C.; Tidwell, Richard R.; Hall, James E.; Wilson, W. David; Kumar, Arvind; Blagburn, Byron L.
PATENT ASSIGNEE(S): Georgia State University Research Foundation, Inc., USA; University of North Carolina at Chapel Hill; Auburn University
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9615126	A1	19960523	WO 1995-US14893	1995 1113

W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ

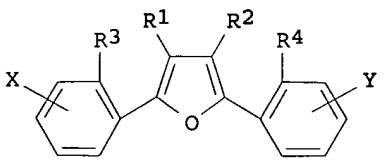
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5602172	A	19970211	US 1995-453276	1995 0530
IL 115875	A1	20001206	IL 1995-115875	1995 1105
CA 2204898	AA	19960523	CA 1995-2204898	1995 1113
AU 9642838	A1	19960606	AU 1996-42838	1995 1113
AU 692024	B2	19980528		
EP 792271	A1	19970903	EP 1995-941407	1995 1113
EP 792271	B1	20020227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10508857	T2	19980902	JP 1995-516327	1995 1113
AT 213737	E	20020315	AT 1995-941407	1995 1113
ES 2173988	T3	20021101	ES 1995-941407	1995 1113
ZA 9509661	A	19960529	ZA 1995-9661	1995 1114

PRIORITY APPLN. INFO.:	US 1994-339487	A1	1994 1114
	US 1994-238766	A2	1994 0506
	WO 1995-US14893	W	1995 1113

OTHER SOURCE(S): MARPAT 125:114460

GI



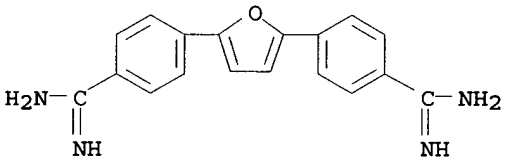
I

AB I [R1, R2 = H, lower alkyl, aryl, alkylaryl, aminoalkyl, aminoaryl, halo, oxyalkyl, oxyaryl, oxyarylalkyl; R3, R4 = H, lower alkyl, oxyalkyl, alkylaryl, aryl, oxyaryl, aminoalkyl, aminoaryl, halo; X and Y are located in the para or meta positions and are selected from H, lower alkyl, oxyalkyl, C(:NR5)NR5R6 (R5 = H, lower alkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, alkylaryl; R5R5 = C2-C10 alkyl,

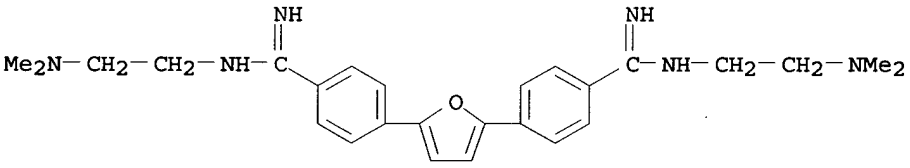
hydroxyalkyl, alkylene; R6 = H, hydroxy, lower alkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylamino, alkylaminoalkyl, cycloalkyl, hydroxycycloalkyl, alkoxycycloalkyl, aryl, alkylaryl)] were prepared as inhibiting agents for pneumocystis carinii pneumonia, giardia lamblia, and cryptosporidium parvum. E.g., 2,5-bis(p-bromophenyl)furan was treated with Cu(CN) in quinoline, and the mixture poured into dilute HCl solution A solution of the bisnitrile in dioxane/EtOH was saturated with dry HCl, and the resulting imidate ester hydrochloride treated with anhydrous NH3 in absolute EtOH to give 2,5-bis(4-amidinophenyl)furan dihydrochloride.

IT **73819-26-8P 166601-09-8P 166601-10-1P 166601-11-2P 173420-56-9P 173420-67-2P 179118-06-0P 179118-08-2P 179118-09-3P 179118-22-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of furan derivs. for inhibition of pneumocystis carinii pneumonia, giardia lamblia, and cryptosporidium parvum)

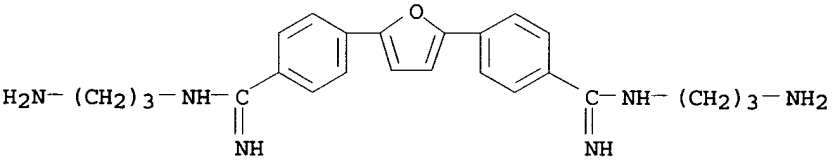
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



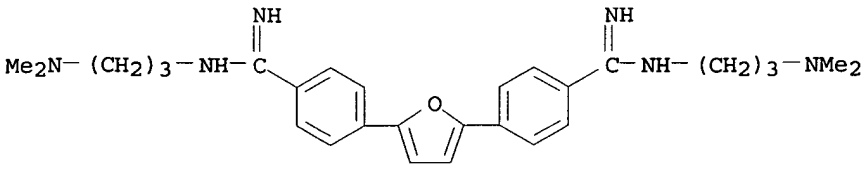
RN 166601-09-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



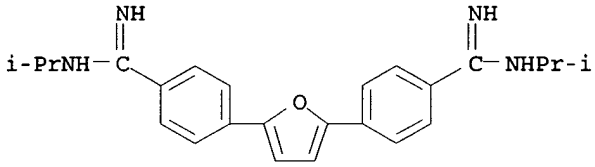
RN 166601-10-1 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(3-aminopropyl)- (9CI) (CA INDEX NAME)



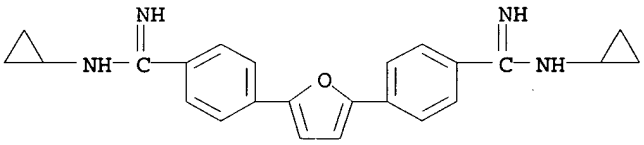
RN 166601-11-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



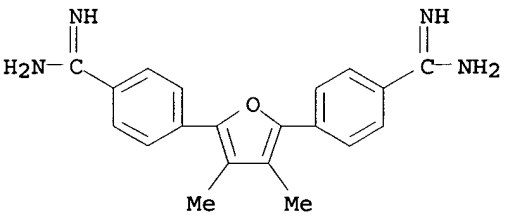
RN 173420-56-9 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)-
(9CI) (CA INDEX NAME)



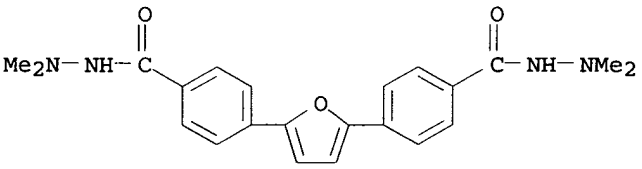
RN 173420-67-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-cyclopropyl-
(9CI) (CA INDEX NAME)



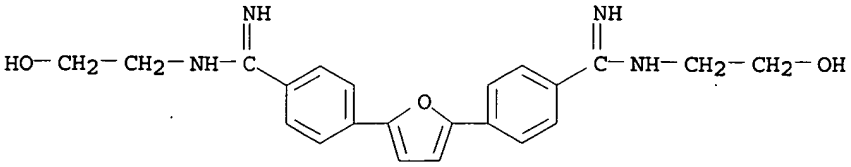
RN 179118-06-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3,4-dimethyl-2,5-furandiyl)bis-
(9CI) (CA INDEX NAME)



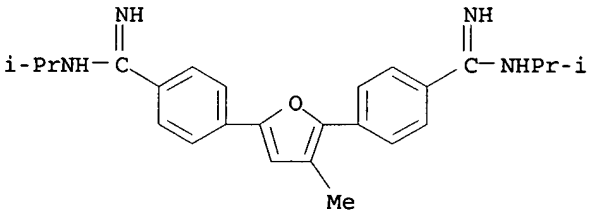
RN 179118-08-2 HCAPLUS
CN Benzoic acid, 4,4'-(2,5-furandiyl)bis-, bis(2,2-dimethylhydrazide)
(9CI) (CA INDEX NAME)



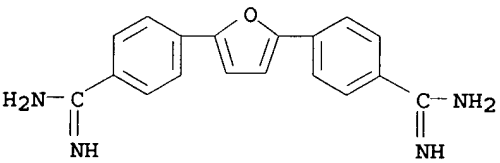
RN 179118-09-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(2-hydroxyethyl)-
(9CI) (CA INDEX NAME)



RN 179118-22-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(3-methyl-2,5-furandiyl)bis[N-(1-
methylethyl)- (9CI) (CA INDEX NAME)

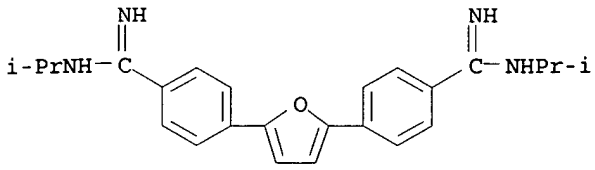


IT **55368-40-6P 173420-57-0P 173420-68-3P**
179118-15-1P 179118-16-2P 179118-17-3P
179118-18-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of furan derivs. for inhibition of pneumocystis carinii
pneumonia, giardia lamblia, and cryptosporidium parvum)
RN 55368-40-6 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis-, dihydrochloride
(9CI) (CA INDEX NAME)



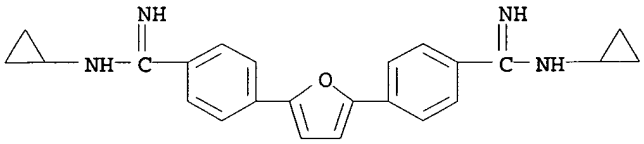
●2 HCl

RN 173420-57-0 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-methylethyl)-
, dihydrochloride (9CI) (CA INDEX NAME)



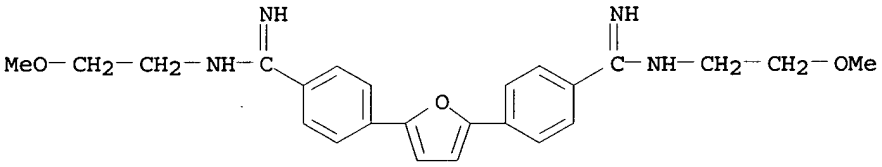
●2 HCl

RN 173420-68-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-cyclopropyl-, dihydrochloride (9CI) (CA INDEX NAME)

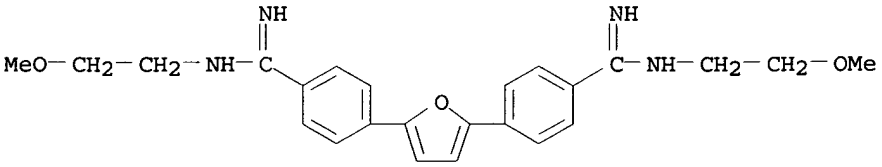


●2 HCl

RN 179118-15-1 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(2-methoxyethyl)- (9CI) (CA INDEX NAME)

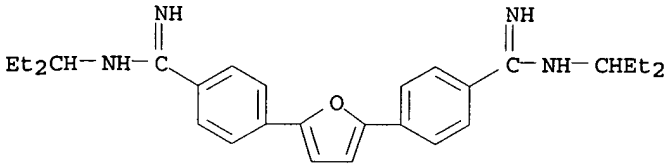


RN 179118-16-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(2-methoxyethyl)-, dihydrochloride (9CI) (CA INDEX NAME)

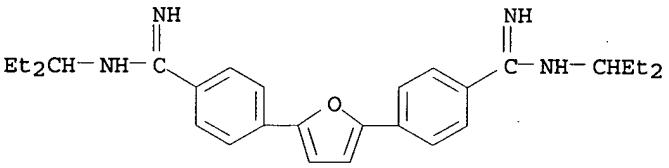


●2 HCl

RN 179118-17-3 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-ethylpropyl)- (9CI) (CA INDEX NAME)



RN 179118-18-4 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(1-ethylpropyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

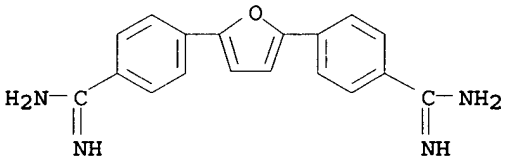
IC ICM C07D405-14
ICS A61K031-415; C07D307-54; A61K031-34
CC 27-6 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 10
ST furan aryl deriv prepn; protozoacide diarylfuran; **microbicide** diarylfuran
IT **73819-26-8P** 80498-71-1P 80498-74-4P 166601-05-4P **166601-09-8P** **166601-10-1P** **166601-11-2P** **173420-56-9P** 173420-58-1P 173420-61-6P **173420-67-2P** 179118-03-7P 179118-04-8P 179118-05-9P **179118-06-0P** 179118-07-1P **179118-08-2P** **179118-09-3P** 179118-10-6P **179118-22-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of furan derivs. for inhibition of pneumocystis carinii pneumonia, giardia lamblia, and cryptosporidium parvum)
IT **55368-40-6P** 61829-76-3P 61880-90-8P 162438-59-7P 162438-60-0P 162438-61-1P 162438-62-2P **173420-57-0P** 173420-60-5P **173420-68-3P** **179118-15-1P** **179118-16-2P** **179118-17-3P** **179118-18-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of furan derivs. for inhibition of pneumocystis carinii pneumonia, giardia lamblia, and cryptosporidium parvum)

L42 ANSWER 38 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:691473 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 123:132012
TITLE: Small changes in cationic substituents of diphenylfuran derivatives have major effects on the binding affinity and the binding mode with RNA helical duplexes
AUTHOR(S): Zhao, Min; Ratmeyer, Lynda; Peloquin, Robert G.; Yao, Shijie; Kumar, Arvind; Spychala, Jaroslaw; Boykin, David W.; Wilson, W. David
CORPORATE SOURCE: Center Biotechnology and Drug Design, Georgia State University, Atlanta, GA, 30303, USA

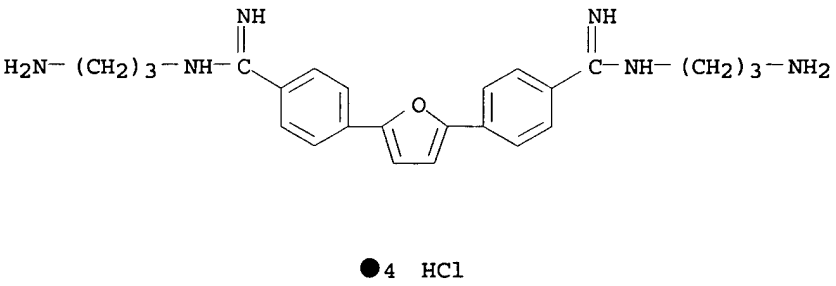
SOURCE: Bioorganic & Medicinal Chemistry (1995), 3(6), 785-94
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Pergamon
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interactions of dicationic and tetracationic diphenylfuran analogs of the **antimicrobial** furamidine with RNA have been analyzed by thermal melting, spectroscopic, viscometric, kinetic and mol.-modeling techniques. The results of these studies indicate that most of the furan derivs. bind to RNA duplexes by intercalation in contrast to their minor-groove binding mode in AT sequences of DNA, but similar to their binding mode in GC rich regions of DNA. The highest affinity for RNA is found for an imidazoline dication. With some substituents which inhibit formation of a strong intercalation complex, the results suggest a non-intercalative type of binding occurs. The non-intercalative binding probably occurs through a complex with the furan derivative bound in the narrow, deep major groove of A-form RNA helixes.

IT **73819-26-8D**, analogs
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interaction of cationic diphenylfuran analogs of **antimicrobial** furamidine with RNA and DNA)
RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



IT **166601-06-5P 166601-07-6P 166601-08-7P**
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(interaction of cationic diphenylfuran analogs of **antimicrobial** furamidine with RNA and DNA)
RN 166601-06-5 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-(3-aminopropyl)-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

RN 166601-07-6 HCAPLUS
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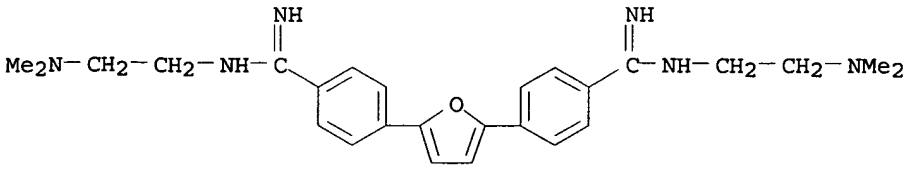

●4 HCl

RN 166601-08-7 HCAPLUS
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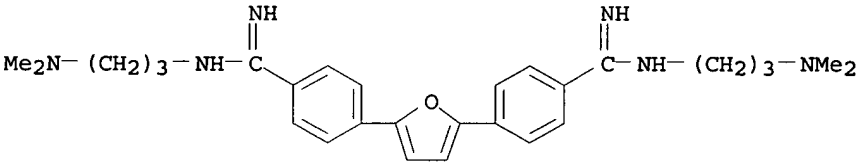
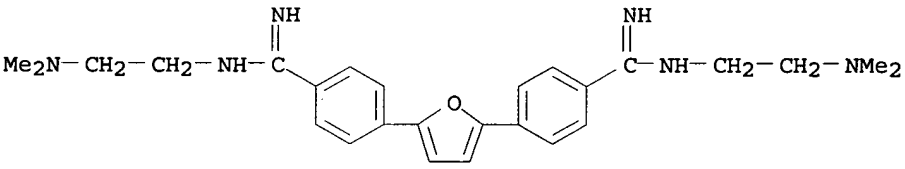


●4 HCl

IT **166601-09-8P 166601-10-1P 166601-11-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(interaction of cationic diphenylfuran analogs of **antimicrobial** furamidine with RNA and DNA)
RN 166601-09-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)



RN 166601-10-1 HCAPLUS
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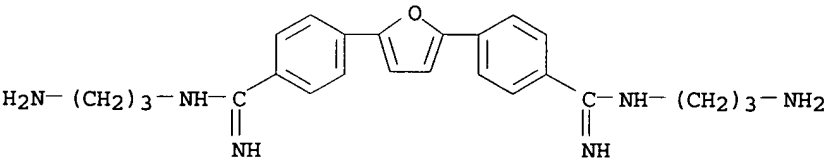
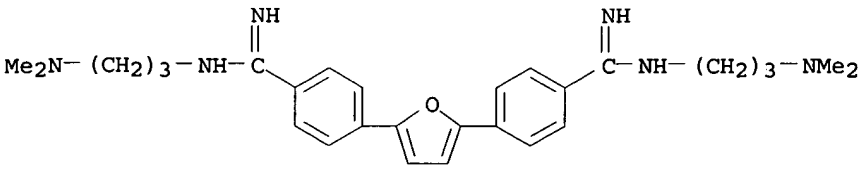


RN 166601-11-2 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis[N-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



CC 1-3 (Pharmacology)
ST diphenylfuran deriv RNA binding; **antimicrobial** furamidine analog RNA binding
IT Deoxyribonucleic acids
Ribonucleic acids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interaction of cationic diphenylfuran analogs of **antimicrobial** furamidine with RNA and DNA)
IT Molecular association
(intercalation, interaction of cationic diphenylfuran analogs of **antimicrobial** furamidine with RNA and DNA)
IT Anti-infective agents
(medical, interaction of cationic diphenylfuran analogs of **antimicrobial** furamidine with RNA and DNA)
IT 24936-38-7, PolyA-polyU 24939-09-1, PolydA-polydT
73819-26-8D, analogs 80498-71-1 80498-74-4
155791-82-5 166601-05-4
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interaction of cationic diphenylfuran analogs of **antimicrobial** furamidine with RNA and DNA)
IT **166601-06-5P 166601-07-6P 166601-08-7P**
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(interaction of cationic diphenylfuran analogs of **antimicrobial** furamidine with RNA and DNA)
IT 108-00-9, N,N-Dimethylethylenediamine 109-76-2, 1,3-Propanediamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(interaction of cationic diphenylfuran analogs of **antimicrobial** furamidine with RNA and DNA)
IT **166601-09-8P 166601-10-1P 166601-11-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(interaction of cationic diphenylfuran analogs of **antimicrobial** furamidine with RNA and DNA)

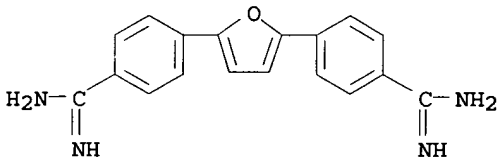
L42 ANSWER 39 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:413305 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 122:230122
TITLE: Dicationic Diarylfurans as Anti-Pneumocystis carinii Agents
AUTHOR(S): Boykin, David W.; Kumar, Arvind; Spychala, Jaroslaw; Zhou, Min; Lombardy, Richard J.; Wilson, W. David; Dykstra, Christine C.; Jones, Susan K.; Hall, James E.; et al.
CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Journal of Medicinal Chemistry (1995), 38(6), 912-16
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Seven dicationic 2,5-diarylfurans have been synthesized, and their interactions with poly(dA-dT) and the duplex oligomer d(CGCCAATTCGCG)2 were evaluated by Tm measurements. The inhibition of topoisomerase II isolated from Giardia lamblia, the inhibition of growth of G. lamblia in cell culture by these furans, and the effectiveness of these compds. against Pneumocystis carinii in the immunosuppressed rat model have been assessed. Strong binding affinities to poly(dA-dT) and to the oligomer were observed for the dicationic furans, and the interaction strength is directly correlated to the biol. activity of the compds. An x-ray structure for the complex of the dicationic amidine derivative, 2,5-bis(4-guanylphenyl)furan (I), with the oligomer demonstrates the snug fit of these compds. with the AATT minor-groove binding site and hydrogen bonds to AT base pairs at the floor of the minor groove. The stronger DNA binding mols. are the most effective inhibitors of topoisomerase II and G. lamblia in cell culture, and there is a correlation for both DNA interaction and topoisomerase II inhibition with the biol. activity of these compds. against G. lamblia. I is the most effective against P. carinii, it is more active and less toxic than pentamidine on i.v. administration and it is also effective by oral dosage. The results presented here suggests a model for the biol. action of these compds. in which the dication first binds in the minor groove of DNA and forms a complex that results in the inhibition of the **microbial** topoisomerase II enzyme.

IT **55368-40-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation, DNA binding, and structure activity relations of dicationic diarylfurans as anti-Pneumocystis carinii agents)

RN 55368-40-6 HCAPLUS

CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

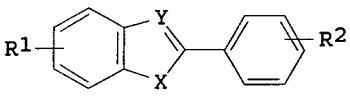
CC 1-3 (Pharmacology)

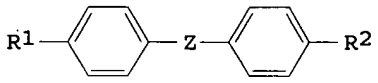
IT Giardia lamblia
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation, DNA binding, and structure-**antimicrobial** activity relations of dicationic diarylfurans)

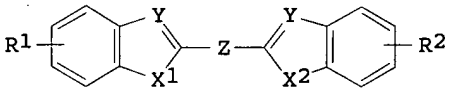
IT 142805-56-9, Topoisomerase II
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of **microbial** topoisomerase II by dicationic diarylfurans and anti-Giardia lamblia activity)

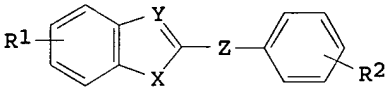
IT **55368-40-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation, DNA binding, and structure activity relations of dicationic diarylfurans as anti-Pneumocystis carinii agents)

L42 ANSWER 40 OF 40 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:57949 HCAPLUS <<LOGINID::20060221>>
DOCUMENT NUMBER: 94:57949
TITLE: Antifungal and antibacterial activities of diarylamidine derivatives
AUTHOR(S): Anne, Jozef; De Clercq, Erik; Eyssen, Hendrik; Dann, Otto
CORPORATE SOURCE: Rega Inst. Med. Res., Katholieke Univ. Leuven, Louvain, B-3000, Belg.
SOURCE: Antimicrobial Agents and Chemotherapy (1980), 18(2), 231-9
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I


II


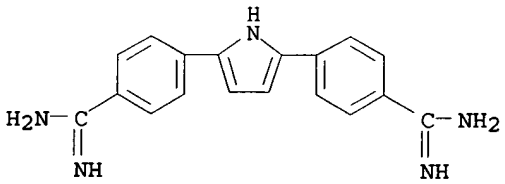
III


IV

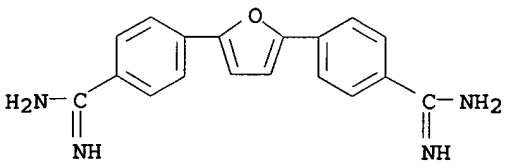
AB Seventy-nine title compds. most of which are described by I, II, III, and IV [R1 and R2 = C(:NH)NH2, imidazolino, etc.; X, X1, X2 = NH, O, S, etc.; Y = CH, CNH2, CMe, N; Z = CH:CH, NHN:N, C6H4O, NHCOC6H4CONH-4, etc.] were evaluated for antibacterial and antifungal activities. Minor structural variations resulted in significant changes of **antimicrobial** activity. In general the structural features required for antifungal activity coincided with those required for antibacterial activity. The most active antifungal compound III (R1 = R2 = amidino, X = NH, Y = CH, and Z = p-C6H4O) was evaluated for its activity against Candida albicans infection in mice.

IT **66639-43-8 73819-26-8 73819-28-0**
RL: BIOL (Biological study)
(bactericidal and fungicidal activity)

RN 66639-43-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(1H-pyrrole-2,5-diyl)bis- (9CI) (CA INDEX NAME)



RN 73819-26-8 HCAPLUS
CN Benzenecarboximidamide, 4,4'-(2,5-furandiyl)bis- (9CI) (CA INDEX NAME)



RN 73819-28-0 HCAPLUS
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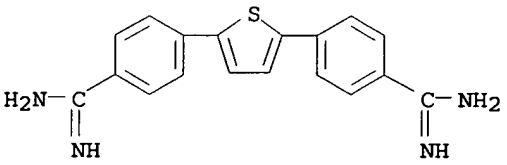

CC 1-3 (Pharmacodynamics)
IT 140-59-0 140-64-7 908-54-3 3602-01-5 4816-14-2 4816-15-3
4816-17-5 13202-07-8 26070-72-4 26070-75-7 47165-00-4
47165-04-8 64431-93-2 65426-89-3 65426-90-6 66638-98-0
66638-99-1D, derivs. 66639-01-8 66639-06-3 66639-09-6
66639-12-1 66639-14-3 66639-15-4 66639-23-4
66639-43-8 66639-67-6 66686-38-2 67684-70-2
73819-17-7 73819-18-8 73819-19-9 73819-20-2 73819-21-3
73819-22-4 73819-23-5 73819-24-6 73819-25-7
73819-26-8 73819-27-9 **73819-28-0** 73819-29-1
73819-30-4 73819-31-5 73819-32-6 73819-33-7 73819-34-8
73819-35-9 73819-36-0 73819-37-1 73819-38-2 73819-39-3
73819-40-6 73819-41-7 73819-42-8 73819-43-9 73819-45-1
73819-46-2 73819-47-3 73819-48-4 73819-49-5 73819-50-8
73819-51-9 73819-52-0 73819-53-1 73819-54-2 73819-55-3
73819-56-4 73819-57-5 73819-58-6 73819-59-7 73819-60-0
73819-61-1 73819-62-2 73819-63-3 73819-64-4 73827-21-1
75746-30-4 75746-31-5
RL: BIOL (Biological study)
(bactericidal and fungicidal activity)

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